Access DB#_____

# SEARCH REQUEST FORM

## Scientific and Technical Information Center

Requester's full Name: Everett White Examiner #: 67057 Date: 9/23/2002
Art Unit: 1623 Phone Number 308-4621 Serial Number: 09/830,761
Mail Box: CM1-8B19 and Bldg/Room Location: CM1-7B13 Results Format Preferred (circle): PAPER DISK E-MAIL

**If more than one search is submitted, please prioritize searches in order of need.**

**********

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be search Include the elected species or structures, key words, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: See Bib Data Sheet

Inventors (please provide full names): See Bib Data Sheet

Earliest priority Filing Date: See Bib Data Sheet

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search the cross-linked hyaluronic acids of Claims 1-4, 12 and 13, the pharmaceutcal composition thereof of Claim 15, a metal complex of a cross-linked hyaluronic acid of Claim 14, and the vascular prosthesis of Claim 16. Note the formula of the diamine set forth in Claims 3 and 4. A copy of the claims is provided.

The Bib Data Sheet which discloses the inventor names, title of the invention, and the earliest priority filing date is also provided.

**********

**STAFF USE ONLY**

Point of Contact:
Alexandra Waclawiw
Technical Info. Specialist
Tel: 308-4491
CM1 6A02

| | Type of Search | Vendors and cost where applicable |
|---|---|---|
| Searcher: | NA Sequence (#)____ | STN_____ |
| Searcher Phone #: | AA Sequence (#)____ | Dialog_____ |
| Searcher Location: | Structure (#) _____ | Questel/Orbit_____ |
| Date Searcher Picked Up: | Bibliographic _____ | Dr. Link_____ |
| Date Completed: | Litigation _____ | Lexis/Nexis_____ |
| Searcher Prep & Review Time: | Fulltext _____ | Sequence Systems_____ |
| Clerical prep time: | Patent Family_____ | WWW/Internet_____ |
| Online Time: | Other _____ | Other (specify)_____ |

PTO-1590 (1-2000)

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=> d his


     FILE 'REGISTRY' ENTERED AT 09:43:56 ON 30 SEP 2002
                E HYALURANIC ACID/CN
                E HYALURONIC ACID/CN
L1            1 S E3
                E HYALURONIC ACID, ION/CN
L2            1 S E4
L3          284 S 9004-61-9/CRN
L4           14 S 54597-23-8/CRN
L5          298 S L3 OR L4
L6        81451 S C2H4O
L7        46784 S C3H6O
L8            7 S L5 AND (L6 OR L7)
L9           63 S L5 AND PMS/CI
L10          22 S L9 AND N>1
L11           1 S L10 AND M/ELS
                E POLYOTHER/PCT
L12      202145 S POLYOTHER/PCT
                E POLYAMINE/PCT
L13       35921 S POLYAMINE/PCT
L14      220446 S POLYETHER/PCT
L15          37 S L9 AND (L12 OR L13 OR L14)
L16          16 S L15 AND L10
L17          20 S L16 OR L11 OR L8

     FILE 'HCAPLUS' ENTERED AT 09:54:59 ON 30 SEP 2002
L18          10 S L17
L19        8923 S L1 OR L2
L20        9833 S L19 OR HYALURONIC ACID
L21       33064 S POLYAMINE# OR POLY (L) AMINE#
L22      151429 S CROSSLINK? OR CROSS LINK?
L23         183 S L20 (L) L22
L24           1 S L23 (L) L21
L25      218751 S AMINE#
L26           2 S L23 (L) L25
L27          12 S L18 OR L24 OR L26
L28       26227 S (POLYAMINE# OR POLY (2A) AMINE#)/AB
L29           2 S L28 AND L23
L30          13 S L29 OR L27


=> fil reg
FILE 'REGISTRY' ENTERED AT 10:18:39 ON 30 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   29 SEP 2002  HIGHEST RN 457047-85-7
DICTIONARY FILE UPDATES:  29 SEP 2002  HIGHEST RN 457047-85-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.
```

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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=> d his l1-l17


               E HYALURONIC ACID/CN
L1             1 S E3
                 E HYALURONIC ACID, ION/CN
L2             1 S E4
L3           284 S 9004-61-9/CRN
L4            14 S 54597-23-8/CRN
L5           298 S L3 OR L4
L6         81451 S C2H4O
L7         46784 S C3H6O
L8             7 S L5 AND (L6 OR L7)
L9            63 S L5 AND PMS/CI
L10           22 S L9 AND N>1
L11            1 S L10 AND M/ELS
                 E POLYOTHER/PCT
L12       202145 S POLYOTHER/PCT
                 E POLYAMINE/PCT
L13        35921 S POLYAMINE/PCT
L14       220446 S POLYETHER/PCT
L15           37 S L9 AND (L12 OR L13 OR L14)
L16           16 S L15 AND L10
L17           20 S L16 OR L11 OR L8

=> d que l1;d l1
L1             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "HYALURONIC ACID"/CN



L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   9004-61-9  REGISTRY
CN   Hyaluronic acid (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   ACP
CN   ACP (polysaccharide)
CN   ACP gel
CN   Durolane
CN   Hyaluronan
CN   Hylartil
CN   Luronit
CN   Mucoitin
CN   Sepracoat
CN   Synvisc
DR   9039-38-7, 37243-73-5, 29382-75-0
MF   Unspecified
CI   PMS, COM, MAN
PCT  Manual registration, Polyester, Polyester formed
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN,
       CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGU,
       DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
       NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, TOXCENTER, USAN,
       USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            8847 REFERENCES IN FILE CA (1962 TO DATE)
             665 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            8856 REFERENCES IN FILE CAPLUS (1962 TO DATE)


=> d que l2;d l2
L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "HYALURONIC ACID, ION
                 (NEG.)"/CN



L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   54597-23-8  REGISTRY
CN   Hyaluronic acid, ion (neg.) (9CI)  (CA INDEX NAME)
MF   Unspecified
CI   COM, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***


=> d que l17
L3           284 SEA FILE=REGISTRY ABB=ON  PLU=ON  9004-61-9/CRN
L4            14 SEA FILE=REGISTRY ABB=ON  PLU=ON  54597-23-8/CRN
L5           298 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 OR L4
L6         81451 SEA FILE=REGISTRY ABB=ON  PLU=ON  C2H4O
L7         46784 SEA FILE=REGISTRY ABB=ON  PLU=ON  C3H6O
L8             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 AND (L6 OR L7)
L9            63 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 AND PMS/CI
L10           22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND N>1
L11            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND M/ELS
L12       202145 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYOTHER/PCT
L13        35921 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYAMINE/PCT
L14       220446 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYETHER/PCT
L15           37 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND (L12 OR L13 OR L14)
L16           16 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 AND L10
L17           20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 OR L11 OR L8


=> d l17 ide can 1-20

L17  ANSWER 1 OF 20  REGISTRY  COPYRIGHT 2002 ACS
RN   354764-92-4  REGISTRY
CN   L-Lysine, polymer with N,N,N-tributyl-1-butanaminium hyaluronate (9CI)
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1-Butanaminium, N,N,N-tributyl-, hyaluronate, polymer with L-lysine (9CI)
CN   Hyaluronic acid, ion (neg.), N,N,N-tributyl-1-butanaminium, polymer with
     L-lysine (9CI)
OTHER NAMES:
CN   Tetrabutylammonium hyaluronate-L-lysine copolymer
FS   STEREOSEARCH
MF   (C16 H36 N . C6 H14 N2 O2 . x Unspecified)x
CI   PMS
PCT  Manual component, Polyamide, Polyamide formed, Polyother
SR   CA
LC   STN Files:   CA, CAPLUS

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     CRN  56-87-1
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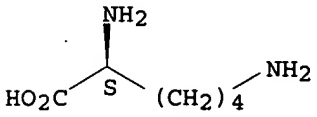
CMF C6 H14 N2 O2

Absolute stereochemistry.



CM 2

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

CM 3

CRN 54597-23-8
CMF Unspecified
CCI MAN

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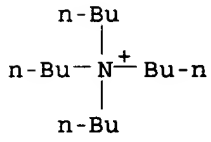
CM 4

CRN 10549-76-5
CMF C16 H36 N



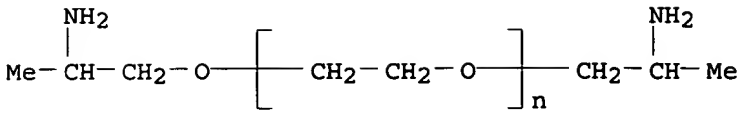
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 135:182285

L17 ANSWER 2 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 292150-06-2 REGISTRY
CN Hyaluronic acid, polymer with .alpha.-(2-aminopropyl)-.omega.-(2-aminopropoxy)poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Poly(oxy-1,2-ethanediyl), .alpha.-(2-aminopropyl)-.omega.-(2-aminopropoxy)-, polymer with hyaluronic acid (9CI)
MF **((C2 H4 O)n C6 H16 N2 O . Unspecified)x**
CI **PMS**
PCT Manual component, Polyester, Polyester formed, **Polyether**
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 70939-81-0
CMF (C2 H4 O)n C6 H16 N2 O
CCI PMS



CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 133:227675

L17 ANSWER 3 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 292150-05-1 REGISTRY
CN Hyaluronic acid, polymer with 1,6-hexanediamine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,6-Hexanediamine, polymer with hyaluronic acid (9CI)
MF **(C6 H16 N2 . Unspecified)x**
CI **PMS**
PCT Manual component, Polyester, Polyester formed, **Polyother**
SR CA
LC STN Files: CA, CAPLUS

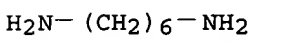
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 124-09-4
CMF C6 H16 N2



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 133:227675

L17 ANSWER 4 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 292150-04-0 REGISTRY
CN Hyaluronic acid, polymer with 1,3-propanediamine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,3-Propanediamine, polymer with hyaluronic acid (9CI)
MF **(C3 H10 N2 . Unspecified)x**
CI **PMS**
PCT Manual component, Polyester, Polyester formed, **Polyother**

SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 109-76-2
CMF C3 H10 N2



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 133:227675

L17 ANSWER 5 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 287485-04-5 REGISTRY
CN Hyaluronic acid, polymer with 2,2'-(1,4-butanediyl)bis[oxirane], ethenol and pentanedial (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethenol, polymer with 2,2'-(1,4-butanediyl)bis[oxirane], hyaluronic acid and pentanedial (9CI)
CN Oxirane, 2,2'-(1,4-butanediyl)bis-, polymer with ethenol, hyaluronic acid and pentanedial (9CI)
CN Pentanedial, polymer with 2,2'-(1,4-butanediyl)bis[oxirane], ethenol and hyaluronic acid (9CI)
MF **(C8 H14 O2 . C5 H8 O2 . C2 H4 O . Unspecified)x**
CI PMS
PCT Epoxy resin, Manual component, Polyester, Polyester formed, Polyether, Polyether formed, Polyvinyl
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

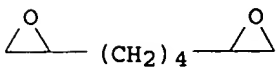
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

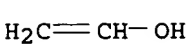
CM 2

CRN 2426-07-5
CMF C8 H14 O2



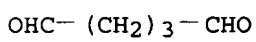
CM 3

CRN 557-75-5
CMF C2 H4 O



CM 4

CRN 111-30-8
CMF C5 H8 O2



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 133:152210

L17 ANSWER 6 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 287485-03-4 REGISTRY
CN Hyaluronic acid, polymer with 2,2'-(1,4-butanediyl)bis[oxirane] and ethenol (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethenol, polymer with 2,2'-(1,4-butanediyl)bis[oxirane] and hyaluronic acid (9CI)
CN Oxirane, 2,2'-(1,4-butanediyl)bis-, polymer with ethenol and hyaluronic acid (9CI)
MF **(C8 H14 O2 . C2 H4 O . Unspecified)x**
CI PMS
PCT Epoxy resin, Manual component, Polyester, Polyester formed, Polyvinyl
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

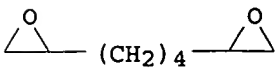
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 2426-07-5
CMF C8 H14 O2



CM 3

CRN 557-75-5

CMF C2 H4 O

$H_2C{=}CH{-}OH$

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 133:152210

L17 ANSWER 7 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 276670-33-8 REGISTRY
CN Hyaluronic acid, polymer with 2,4-diisocyanato-1-methylbenzene and KE 825 (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzene, 2,4-diisocyanato-1-methyl-, polymer with hyaluronic acid and KE 825 (9CI)
CN KE 825, polymer with 2,4-diisocyanato-1-methylbenzene and hyaluronic acid (9CI)
OTHER NAMES:
CN Hyaluronic acid-KE 825-toluene-2,4-diisocyanate copolymer
MF **(C9 H6 N2 O2 . Unspecified . Unspecified)x**
CI **PMS**
PCT Manual component, Polyester, Polyester formed, **Polyother**, Polyurethane, Polyurethane formed
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 276670-09-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 584-84-9
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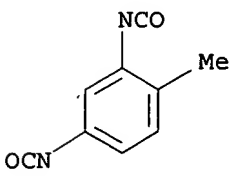


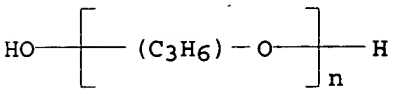

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 133:64095

L17 ANSWER 8 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 275816-50-7 REGISTRY
CN Hyaluronic acid, polymer with .alpha.-hydro-.omega.-hydroxypoly[oxy(methyl-1,2-ethanediyl)] and 1,1'-methylenebis[4-isocyanatobenzene] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzene, 1,1'-methylenebis[4-isocyanato-, polymer with hyaluronic acid and .alpha.-hydro-.omega.-hydroxypoly[oxy(methyl-1,2-ethanediyl)] (9CI)
CN Poly[oxy(methyl-1,2-ethanediyl)], .alpha.-hydro-.omega.-hydroxy-, polymer with hyaluronic acid and 1,1'-methylenebis[4-isocyanatobenzene] (9CI)
OTHER NAMES:
CN Hyaluronic acid-4,4'-methylenebis(phenylisocyanate)-polypropylene glycol copolymer
MF **(C15 H10 N2 O2 . (C3 H6 O)n H2 O . Unspecified)x**
CI **PMS**
PCT Manual component, Polyester, Polyester formed, **Polyether**, Polyurethane, Polyurethane formed
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 25322-69-4
CMF (C3 H6 O)n H2 O
CCI IDS, PMS



CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

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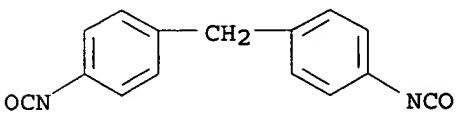
CRN 101-68-8
CMF C15 H10 N2 O2



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 133:64095

L17 ANSWER 9 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 267882-34-8 REGISTRY
CN Hyaluronic acid, ion (neg.), N,N,N-tributyl-1-butanaminium, polymer with 1,3-propanediamine, copper salt (9CI) (CA INDEX NAME)

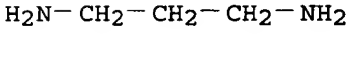
OTHER CA INDEX NAMES:
CN 1,3-Propanediamine, polymer with N,N,N-tributyl-1-butanaminium hyaluronate, copper salt (9CI)
CN 1-Butanaminium, N,N,N-tributyl-, hyaluronate, Polymer with 1,3-propanediamine, copper salt (9CI)
MF **(C16 H36 N . C3 H10 N2 . x Unspecified)x . x Cu**
PCT Manual component, **Polyother**, Polyother only
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 267882-30-4
CMF (C16 H36 N . C3 H10 N2 . x Unspecified)x
CCI PMS

CM 2

CRN 109-76-2
CMF C3 H10 N2



CM 3

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

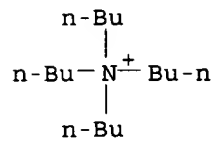
CM 4

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 5

CRN 10549-76-5
CMF C16 H36 N



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

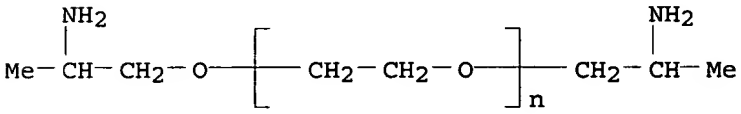
REFERENCE 1: 132:336032

L17 ANSWER 10 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 267882-33-7 REGISTRY
CN Hyaluronic acid, ion (neg.), N,N,N-tributyl-1-butanaminium, polymer with .alpha.-(2-aminopropyl)-.omega.-(2-aminopropoxy)poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN 1-Butanaminium, N,N,N-tributyl-, hyaluronate, polymer with .alpha.-(2-aminopropyl)-.omega.-(2-aminopropoxy)poly(oxy-1,2-ethanediyl) (9CI)
CN Poly(oxy-1,2-ethanediyl), .alpha.-(2-aminopropyl)-.omega.-(2-aminopropoxy)-, polymer with N,N,N-tributyl-1-butanaminium hyaluronate (9CI)
MF **(C16 H36 N . (C2 H4 O)n C6 H16 N2 O . x Unspecified)x**
CI **PMS**
PCT Manual component, **Polyether, Polyother**
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 70939-81-0
CMF (C2 H4 O)n C6 H16 N2 O
CCI PMS



CM 2

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

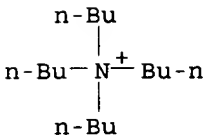
CM 3

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

CRN 10549-76-5
CMF C16 H36 N



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

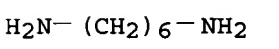
REFERENCE 1: 132:336032

L17 ANSWER 11 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 267882-32-6 REGISTRY
CN Hyaluronic acid, ion (neg.), N,N,N-tributyl-1-butanaminium, polymer with 1,6-hexanediamine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,6-Hexanediamine, polymer with N,N,N-tributyl-1-butanaminium hyaluronate (9CI)

CN 1-Butanaminium, N,N,N-tributyl-, hyaluronate, polymer with 1,6-hexanediamine (9CI)
MF **(C16 H36 N . C6 H16 N2 . x Unspecified)x**
CI **PMS**
PCT Manual component, **Polyother**, Polyother only
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 124-09-4
CMF C6 H16 N2



CM 2

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

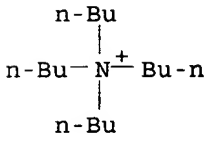
CM 3

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

CRN 10549-76-5
CMF C16 H36 N



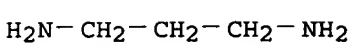
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:336032

L17 ANSWER 12 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 267882-30-4 REGISTRY
CN Hyaluronic acid, ion( neg.), N,N,N-tributyl-1-butanaminium, polymer with 1,3-propanediamine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,3-Propanediamine, polymer with N,N,N-tributyl-1-butanaminium hyaluronate (9CI)
CN 1-Butanaminium, N,N,N-tributyl-, hyaluronate, polymer with 1,3-propanediamine (9CI)
MF **(C16 H36 N . C3 H10 N2 . x Unspecified)x**
CI **PMS, COM**
PCT Manual component, **Polyother**, Polyother only
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 109-76-2
CMF C3 H10 N2



CM 2

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

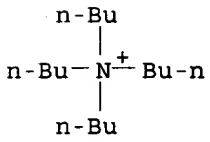
CM 3

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

CRN 10549-76-5
CMF C16 H36 N



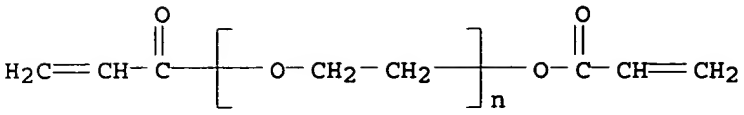
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:336032

L17 ANSWER 13 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 202935-06-6 REGISTRY
CN Hyaluronic acid, 2-propenoate, carboxymethyl ether, polymer with .alpha.-(1-oxo-2-propenyl)-.omega.-[(1-oxo-2-propenyl)oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxo-2-propenyl)-.omega.-[(1-oxo-2-propenyl)oxy]-, polymer with hyaluronic acid 2-propenoate carboxymethyl ether (9CI)
MF **(C3 H4 O2 . x C2 H4 O3 . (C2 H4 O)n C6 H6 O3 . x Unspecified)x**
CI PMS
PCT Manual component, Polyacrylic, Polyester, Polyester formed, Polyether
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 26570-48-9
CMF (C2 H4 O)n C6 H6 O3
CCI PMS



CM 2

CRN 202935-05-5
CMF C3 H4 O2 . x C2 H4 O3 . x Unspecified

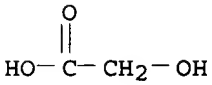
CM 3

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

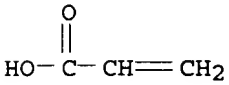
CM 4

CRN 79-14-1
CMF C2 H4 O3



CM 5

CRN 79-10-7
CMF C3 H4 O2



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 128:169784

L17 ANSWER 14 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 188968-25-4 REGISTRY
CN Hyaluronic acid, polymer with hexanedioic acid dihydrazide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Hexanedioic acid, dihydrazide, polymer with hyaluronic acid (9CI)
OTHER NAMES:
CN Adipic dihydrazide-hyaluronic acid copolymer
MF **(C6 H14 N4 O2 . Unspecified)x**
CI **PMS**
PCT Manual component, Polyester, Polyester formed, **Polyother**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

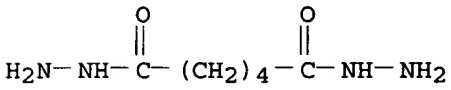
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 1071-93-8
CMF C6 H14 N4 O2



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 126:279255

L17 ANSWER 15 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 188968-15-2 REGISTRY
CN Hyaluronic acid, polymer with 2,3-dihydro-1,4-phthalazinedione dihydrazone (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,4-Phthalazinedione, 2,3-dihydro-, dihydrazone, polymer with hyaluronic acid (9CI)
OTHER NAMES:
CN Hyaluronic acid-1,4-dihydrazinophthalazine copolymer
MF **(C8 H10 N6 . Unspecified)x**
CI **PMS**
PCT Manual component, Polyester, Polyester formed, **Polyother**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

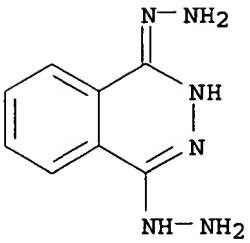
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 484-23-1
CMF C8 H10 N6



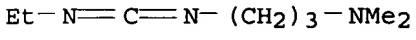
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 126:279255

L17 ANSWER 16 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 165324-67-4 REGISTRY
CN L-Lysine, polymer with N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride and hyaluronic acid (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,3-Propanediamine, N'-(ethylcarbonimidoyl)-N,N-dimethyl-, monohydrochloride, polymer with hyaluronic acid and L-lysine (9CI)
CN Hyaluronic acid, polymer with N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride and L-lysine (9CI)
FS STEREOSEARCH
MF **(C8 H17 N3 . C6 H14 N2 O2 . Cl H . Unspecified)x**
CI **PMS**
PCT Manual component, Polyamide, Polyamide formed, Polyester, Polyester formed, **Polyother**
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 25952-53-8 (1892-57-5)
CMF C8 H17 N3 . Cl H



● HCl

CM 2

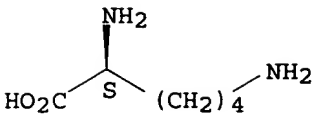
CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.



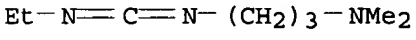
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 123:86466

L17 ANSWER 17 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 165324-66-3 REGISTRY
CN L-Lysine, methyl ester, polymer with N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride and hyaluronic acid (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,3-Propanediamine, N'-(ethylcarbonimidoyl)-N,N-dimethyl-, monohydrochloride, polymer with hyaluronic acid and L-lysine methyl ester (9CI)
CN Hyaluronic acid, polymer with N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride and L-lysine methyl ester (9CI)
FS STEREOSEARCH
MF **(C8 H17 N3 . C7 H16 N2 O2 . Cl H . Unspecified)x**
CI **PMS**
PCT Manual component, Polyamide, Polyamide formed, Polyester, Polyester formed, **Polyother**
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 25952-53-8 (1892-57-5)
CMF C8 H17 N3 . Cl H





CM 2

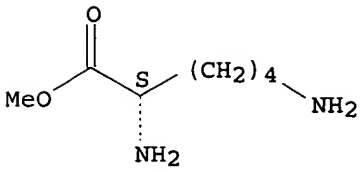
CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 687-64-9
CMF C7 H16 N2 O2

Absolute stereochemistry.



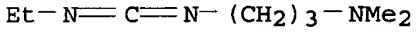
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 123:86466

L17 ANSWER 18 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 165324-65-2 REGISTRY
CN Hyaluronic acid, polymer with N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,3-Propanediamine, N'-(ethylcarbonimidoyl)-N,N-dimethyl-, monohydrochloride, polymer with hyaluronic acid (9CI)
MF **(C8 H17 N3 . Cl H . Unspecified)x**
CI **PMS**
PCT Manual component, Polyester, Polyester formed, **Polyother**
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 25952-53-8 (1892-57-5)
CMF C8 H17 N3 . Cl H



CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 123:86466

L17 ANSWER 19 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 153369-06-3 REGISTRY
CN Hyaluronic acid, 3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinepropanoate (ester), homopolymer (9CI) (CA INDEX NAME)
MF **(C8 H10 N2 O4 . x Unspecified)x**
CI **PMS**
PCT Manual component, Polyester, Polyester formed, **Polyother**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CM 1

CRN 153130-77-9
CMF C8 H10 N2 O4 . x Unspecified

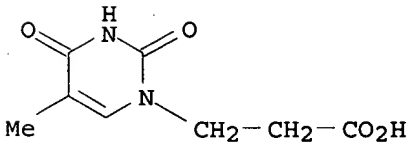
CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 6214-59-1
CMF C8 H10 N2 O4



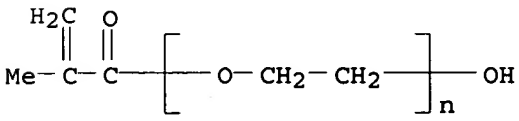
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 120:137558

L17 ANSWER 20 OF 20 REGISTRY COPYRIGHT 2002 ACS
RN 151205-68-4 REGISTRY
CN Hyaluronic acid, polymer with .alpha.-(2-methyl-1-oxo-2-propenyl)-.omega.-hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Poly(oxy-1,2-ethanediyl), .alpha.-(2-methyl-1-oxo-2-propenyl)-.omega.-hydroxy-, polymer with hyaluronic acid (9CI)
MF **((C2 H4 O)n C4 H6 O2 . Unspecified)x**
CI PMS
PCT Manual component, Polyacrylic, Polyester, Polyester formed, Polyether
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 25736-86-1
CMF (C2 H4 O)n C4 H6 O2
CCI PMS



CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
               1 REFERENCES IN FILE CA (1962 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE   1:  119:256535


=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 10:19:50 ON 30 SEP 2002
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FILE COVERS 1907 - 30 Sep 2002  VOL 137 ISS 14
FILE LAST UPDATED: 29 Sep 2002  (20020929/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE


=> d his l18-

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L19        8923 S L1 OR L2
L20        9833 S L19 OR HYALURONIC ACID
L21       33064 S POLYAMINE# OR POLY (L) AMINE#
L22      151429 S CROSSLINK? OR CROSS LINK?
L23         183 S L20 (L) L22
L24           1 S L23 (L) L21
L25      218751 S AMINE#
L26           2 S L23 (L) L25
L27          12 S L18 OR L24 OR L26
L28       26227 S (POLYAMINE# OR POLY (2A) AMINE#)/AB
L29           2 S L28 AND L23
L30          13 S L29 OR L27


=> d que  l30
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L2            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "HYALURONIC ACID, ION
                (NEG.)"/CN
L3          284 SEA FILE=REGISTRY ABB=ON  PLU=ON  9004-61-9/CRN
L4           14 SEA FILE=REGISTRY ABB=ON  PLU=ON  54597-23-8/CRN
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L5          298 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 OR L4
L6        81451 SEA FILE=REGISTRY ABB=ON  PLU=ON  C2H4O
L7        46784 SEA FILE=REGISTRY ABB=ON  PLU=ON  C3H6O
L8            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 AND (L6 OR L7)
L9           63 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 AND PMS/CI
L10          22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND N>1
L11           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND M/ELS
L12      202145 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYOTHER/PCT
L13       35921 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYAMINE/PCT
L14      220446 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYETHER/PCT
L15          37 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND (L12 OR L13 OR L14)
L16          16 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 AND L10
L17          20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 OR L11 OR L8
L18          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17
L19        8923 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR L2
L20        9833 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 OR HYALURONIC ACID/OBI
L21       33064 SEA FILE=HCAPLUS ABB=ON  PLU=ON  POLYAMINE#/OBI OR POLY/OBI
                 (L) AMINE#/OBI
L22      151429 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CROSSLINK?/OBI OR CROSS
                 LINK?/OBI
L23         183 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 (L) L22
L24           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 (L) L21
L25      218751 SEA FILE=HCAPLUS ABB=ON  PLU=ON  AMINE#/OBI
L26           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 (L) L25
L27          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 OR L24 OR L26
L28       26227 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (POLYAMINE# OR POLY (2A)
                 AMINE#)/AB
L29           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 AND L23
L30          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 OR L27


=> d .ca hitstr l30 1-13

L30  ANSWER 1 OF 13  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:293708  HCAPLUS
DOCUMENT NUMBER:          136:311614
TITLE:                    Crosslinked amide derivatives of hyaluronic acid and
                          manufacturing method thereof
INVENTOR(S):              Moon, Tae-Seok; Lee, Jae-Young; Kim, Jin-Hoon; Han,
                          Kyu-Boem
PATENT ASSIGNEE(S):       LG Chem Investment, Ltd., S. Korea
SOURCE:                   PCT Int. Appl., 29 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     WO 2002030990      A1   20020418       WO 2001-KR1687    20011010
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2001094320      A5   20020422       AU 2001-94320     20011010
PRIORITY APPLN. INFO.:                   KR 2000-59443     A  20001010
```

WO 2001-KR1687 W 20011010

AB The present invention relates to water-insol., crosslinked amide derivs. of hyaluronic acid and manufg. method thereof, where the amide derivs. of hyaluronic acid are characterized by crosslinking, of polymer or oligomer having two or more amine groups, e.g., chitosan, with hyaluronic acid or its hyaluronate salts through amidation reaction. The water-insol., crosslinked amide derivs. of hyaluronic acid according to the present invention may be diversely used for prevention of adhesion after surgical operation, correction of facial wrinkles, dermal augmentation, tissue engineering, osteoarthritic visco supplement, etc. (no data).

IC ICM C08B037-08

CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 37, 63

ST **polyamine hyaluronic acid** amide **crosslinking** water insol deriv

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833387 HCAPLUS
DOCUMENT NUMBER: 135:372507
TITLE: Crosslinking of amine-containing polymers with activated dicarboxylic acids
INVENTOR(S): Sportoletti, Giancarlo; Barbucci, Rolando
PATENT ASSIGNEE(S): Aquisitio S.p.A., Italy
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001085801 | A1 | 20011115 | WO 2001-EP5031 | 20010503 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2000-MI1030 A 20000510

AB Polymers contg. primary or secondary amino groups are crosslinked by treating with suitably activated dicarboxylic acids; residual amino groups in the crosslinked polymers can be "quenched". The crosslinked polymers are suitable for the prepn. of pharmaceuticals, cosmetics, or medical/surgical devices. Thus, deacetylated hyaluronic acid was crosslinked with aspartic acid nitrophenyl ester and then quenched with pyridine/SO3 complex.

IC ICM C08B037-08
ICS C08J003-24; C08K005-12

CC 37-6 (Plastics Manufacture and Processing)
Section cross-reference(s): 62, 63

ST **amine** polymer **crosslinking** dicarboxylic acid; **hyaluronic acid crosslinking** aspartic acid

IT **9004-61-9DP**, **Hyaluronic acid**, deacetylated, sulfated
RL: SPN (Synthetic preparation); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(aspartic acid-**crosslinked**; **crosslinking** of

**amine**-contg. polymers with activated dicarboxylic acids and use in pharmaceuticals, cosmetics, and surgical goods)

IT 88879-44-1P
RL: SPN (Synthetic preparation); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(deacetylated **hyaluronic acid crosslinked** by; **crosslinking** of **amine**-contg. polymers with activated dicarboxylic acids and use in pharmaceuticals, cosmetics, and surgical goods)

IT **9004-61-9DP**, **Hyaluronic acid**, deacetylated, sulfated
RL: SPN (Synthetic preparation); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(aspartic acid-**crosslinked**; **crosslinking** of **amine**-contg. polymers with activated dicarboxylic acids and use in pharmaceuticals, cosmetics, and surgical goods)

RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:598045 HCAPLUS
DOCUMENT NUMBER: 135:182285
TITLE: Water-insoluble gels of hyaluronic acid crosslinked with bifunctional L-amino acids or L-amino esters or mixtures thereof
INVENTOR(S): Fratini, Luigi; Meldoli, Maurizio
PATENT ASSIGNEE(S): S.F.I.R. Societa' Fondiaria Industriale Romagnola S.P.A., Italy
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001058961 | A1 | 20010816 | WO 2001-EP1239 | 20010206 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2000-FI20 A 20000208

AB The gels useful for cosmetics and pharmaceuticals are prepd., e.g., by adjusting a soln. of 1 g hyaluronic acid Na salt in 80 mL water to pH 5 with 0.75M HCl, adding 0.58 g N-3-dimethylaminopropylethylcarbodiimide hydrochloride (activator) and 0.44 g L-lysine, dialyzing the reaction mixt. after 2 h and addn. of 80 mL 1M NaCl soln. using water, pptg. with acetone, dissolving in water and freeze drying.

IC ICM C08B037-08
ICS A61K009-36
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 62, 63
IT 354764-88-8P 354764-89-9P 354764-91-3P **354764-92-4P**

354764-93-5P 354764-94-6P 354764-95-7P
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(water-insol. gels of hyaluronic acid crosslinked with bifunctional L-amino acids or L-amino esters or mixts. thereof)

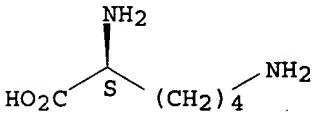
IT **354764-92-4P**
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(water-insol. gels of hyaluronic acid crosslinked with bifunctional L-amino acids or L-amino esters or mixts. thereof)

RN 354764-92-4 HCAPLUS
CN L-Lysine, polymer with N,N,N-tributyl-1-butanaminium hyaluronate (9CI) (CA INDEX NAME)

CM 1

CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.



CM 2

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

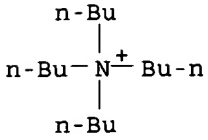
CM 3

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

CRN 10549-76-5
CMF C16 H36 N



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:553605 HCAPLUS
DOCUMENT NUMBER: 133:152210
TITLE: Process for crosslinking hyaluronic acid to polymers

INVENTOR(S): Zhao, Xiaobin; Alexander, Catherine; Fraser, Jane Elizabeth
PATENT ASSIGNEE(S): Fermentech Medical Limited, UK
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000046252 | A1 | 20000810 | WO 2000-GB316 | 20000203 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2000007985 | A | 20011106 | BR 2000-7985 | 20000203 |
| EP 1163274 | A1 | 20011219 | EP 2000-901772 | 20000203 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 2002049281 | A1 | 20020425 | US 2001-924182 | 20010802 |

PRIORITY APPLN. INFO.: GB 1999-2652 A 19990205
WO 2000-GB316 W 20000203

AB The present invention provides a process for the prodn. of hyaluronic acid derivs. cross-linked with another polymer, in particular multiple, e.g., double, crosslinked hyaluronic acid derivs. The invention also provides novel cross-linked derivs., products contg. them and their uses in cosmetic, medical and pharmaceutical applications.

IC ICM C08B037-08
ICS A61L015-28; A61L027-20

CC 44-5 (Industrial Carbohydrates)

IT **287485-03-4P 287485-04-5P** 287485-05-6P, 1,2,7,8-Diepoxyoctane-sodium alginate-sodium hyaluronate copolymer 287485-06-7P, 1,2,7,8-Diepoxyoctane-chitosan-hyaluronic acid copolymer
RL: IMF (Industrial manufacture); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(process for crosslinking hyaluronic acid to polymers)

IT **287485-03-4P 287485-04-5P**
RL: IMF (Industrial manufacture); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(process for crosslinking hyaluronic acid to polymers)

RN 287485-03-4 HCAPLUS

CN Hyaluronic acid, polymer with 2,2'-(1,4-butanediyl)bis[oxirane] and ethenol (9CI) (CA INDEX NAME)

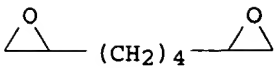
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

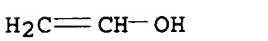
CM 2

CRN 2426-07-5
CMF C8 H14 O2



CM 3

CRN 557-75-5
CMF C2 H4 O



RN 287485-04-5 HCAPLUS
CN Hyaluronic acid, polymer with 2,2'-(1,4-butanediyl)bis[oxirane], ethenol and pentanedial (9CI) (CA INDEX NAME)

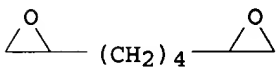
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

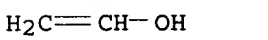
CM 2

CRN 2426-07-5
CMF C8 H14 O2



CM 3

CRN 557-75-5
CMF C2 H4 O



CM 4

CRN 111-30-8
CMF C5 H8 O2



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:468698 HCAPLUS
DOCUMENT NUMBER: 133:227675
TITLE: Synthesis, chemical and rheological characterization of new hyaluronic acid-based hydrogels
AUTHOR(S): Barbucci, R.; Rappuoli, R.; Borzacchiello, A.; Ambrosio, L.
CORPORATE SOURCE: CRISMA and Department of Chemical and Biosystem Sciences and Technologies, University of Siena, Siena, 53100, Italy
SOURCE: Journal of Biomaterials Science, Polymer Edition (2000), 11(4), 383-399
CODEN: JBSEEA; ISSN: 0920-5063
PUBLISHER: VSP BV
DOCUMENT TYPE: Journal
LANGUAGE: English

AB New hyaluronic acid-based hydrogels have been synthesized. The carboxylate groups of hyaluronan were activated in order to bind the amino terminal groups of the di-amine crosslinking reagent. Different hydrogels were obtained according to the different di-amine crosslinking agents (1,3-diaminepropane, 1,6-diaminohexane, PEG500 di-amine, and PEG800 di-amine). The cross-linked polymer (C.L.Hyal) was then sulfated (C.L.HyalS) by a heterogeneous reaction using sulfur trioxide pyridine complex (SO3-Py). The thermo-mech. properties and swelling degree were evaluated and are discussed in relation to the chem. structure and the hydrophilic character of the gels. The different behaviors of C.L.Hyal and C.L.HyalS indicate the important role of sulfated groups.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 35, 38

IT 9004-61-9P, Hyaluronic acid **292150-04-0DP**, sulfated **292150-05-1DP**, sulfated **292150-06-2DP**, sulfated
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, chem. and rheol. characterization of new hyaluronic acid-based hydrogels)

IT **292150-04-0DP**, sulfated **292150-05-1DP**, sulfated **292150-06-2DP**, sulfated
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, chem. and rheol. characterization of new hyaluronic acid-based hydrogels)

RN 292150-04-0 HCAPLUS
CN Hyaluronic acid, polymer with 1,3-propanediamine (9CI) (CA INDEX NAME)

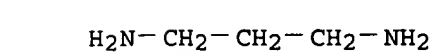
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 109-76-2
CMF C3 H10 N2



RN 292150-05-1 HCAPLUS
CN Hyaluronic acid, polymer with 1,6-hexanediamine (9CI) (CA INDEX NAME)

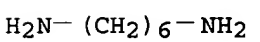
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

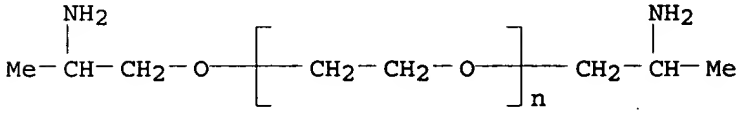
CRN 124-09-4
CMF C6 H16 N2



RN 292150-06-2 HCAPLUS
CN Hyaluronic acid, polymer with .alpha.-(2-aminopropyl)-.omega.-(2-aminopropoxy)poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM 1

CRN 70939-81-0
CMF (C2 H4 O)n C6 H16 N2 O
CCI PMS



CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:412041 HCAPLUS
DOCUMENT NUMBER: 133:64095
TITLE: Wound dressing containing polyurethane foams
INVENTOR(S): Lee, Jae Suk; Cho, Young Sun; Kim, Sun Mi; Park, Myung Hwan; Lee, Jin Woo; Yoon, Taik Lim
PATENT ASSIGNEE(S): Korea Research Institute of Chemical Technology, S. Korea
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

JP 2000167036 A2 20000620 JP 1999-344893 19991203
JP 3304942 B2 20020722
KR 2000038061 A 20000705 KR 1998-52921 19981203
PRIORITY APPLN. INFO.: KR 1998-52921 A 19981203

AB The invention relates to a wound dressing having improved biocompatibility and mech. strength, wherein the dressing contains a polyurethane foam hydrogel prepd. from a polypropylene glycol-contg. polyurethane prepolymer, and a compd. contg. carboxyl and hydroxyl groups 3-10, surfactant 1-6, foaming agent 40-70, antimicrobial agent 0.01-0.1, and crosslinking agent 5-30 % of the prepolymer. A wound dressing was prepd. from polyol (KE 825)-toluene-2,4-diisocyanate (TDI) prepolymer, alginate, polypropylene glycol-polyethylene glycol copolymer surfactant (F 68), water as foaming agent, and silver sulfadiazine (AgSD).

IC ICM A61L015-44
ICS A61K009-70; A61K047-34

CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 37

IT 143502-88-9P, Dimethyloylpropionic acid-4,4'-methlenebis(phenylisocyanate)-polypropylene glycol copolymer 275816-49-4P, Alginic acid-4,4'-methlenebis(phenylisocyanate)-polypropylene glycol copolymer **275816-50-7P**, Hyaluronic acid-4,4'-methlenebis(phenylisocyanate)-polypropylene glycol copolymer 276670-32-7P, Alginic acid-KE-825-toluene-2,4-diisocyanate copolymer **276670-33-8P**, Hyaluronic acid-KE-825-toluene-2,4-diisocyanate copolymer 276679-73-3P, Dimethylolbutanoic acid-4,4'-methlenebis(phenylisocyanate)-polypropylene glycol copolymer
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(wound dressing contg. polyurethane foam hydrogels)

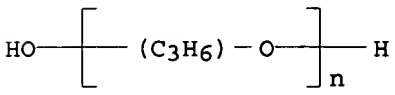
IT **275816-50-7P**, Hyaluronic acid-4,4'-methlenebis(phenylisocyanate)-polypropylene glycol copolymer **276670-33-8P**, Hyaluronic acid-KE-825-toluene-2,4-diisocyanate copolymer
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(wound dressing contg. polyurethane foam hydrogels)

RN 275816-50-7 HCAPLUS

CN Hyaluronic acid, polymer with .alpha.-hydro-.omega.-hydroxypoly[oxy(methyl-1,2-ethanediyl)] and 1,1'-methylenebis[4-isocyanatobenzene] (9CI) (CA INDEX NAME)

CM 1

CRN 25322-69-4
CMF (C3 H6 O)n H2 O
CCI IDS, PMS



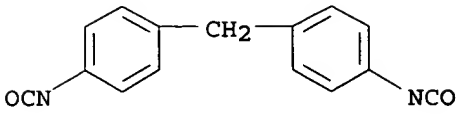

CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 101-68-8
CMF C15 H10 N2 O2




RN 276670-33-8 HCAPLUS
CN Hyaluronic acid, polymer with 2,4-diisocyanato-1-methylbenzene and KE 825 (9CI) (CA INDEX NAME)

CM 1

CRN 276670-09-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

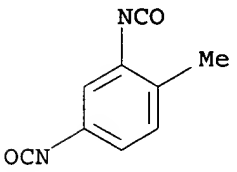
CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 584-84-9
CMF C9 H6 N2 O2




L30 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:335448 HCAPLUS
DOCUMENT NUMBER: 132:336032
TITLE: **Crosslinked hyaluronic acids** and medical uses thereof
INVENTOR(S): Barbucci, Rolando; Rapuoli, Roberto
PATENT ASSIGNEE(S): Aquisitio S.p.A., Italy
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000027887 | A2 | 20000518 | WO 1999-EP8481 | 19991108 |
| WO 2000027887 | A3 | 20001116 | | |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| IT 1303735 | B1 | 20010223 | IT 1998-MI2440 | 19981111 | |
| IT 98MI2440 | A1 | 20000511 | | | |
| BR 9915235 | A | 20010724 | BR 1999-15235 | 19991108 | |
| EP 1144459 | A2 | 20011017 | EP 1999-968778 | 19991108 | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| JP 2002529550 | T2 | 20020910 | JP 2000-581064 | 19991108 | |
| NO 2001002315 | A | 20010706 | NO 2001-2315 | 20010510 | |

PRIORITY APPLN. INFO.: IT 1998-MI2440 A 19981111
WO 1999-EP8481 W 19991108

OTHER SOURCE(S): MARPAT 132:336032

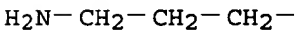
AB Crosslinked hyaluronic acids obtained by reaction of activated carboxylic groups of native linear hyaluronic acid, of extractive or biosynthetic source, with a **polyamine**, particularly a linear alkyl diamine, are useful as substitutes for synovial fluid or vitreous humor, controlled-release matrixes for medicaments, healing and antiadhesive agents, moisturizers, and for the prepn. of vascular prosthesis, biohybrid organs, healing devices, ophthalmic and otol. compns., prosthesis, implants and medical devices. The crosslinking degree can be adjusted by changing the amt. of carboxy-activating agent and is reproducible. The crosslinked hyaluronic acids can optionally be sulfated or hemisuccinylated. Both crosslinked hyaluronic acids and their corresponding sulfate esters lack platelet activation and aggregation. Thus, lyophilized tributylammonium hyaluronate was dissolved in anhyd. DMF, activated with 6 x 10-4 mol chloromethylpyridylium iodide, crosslinked with 0.023 mol 1,6-diaminohexane in the presence of triethylamine, and lyophilized, giving crosslinking degree 50% and swelling degree in water 8.000, water vaporization enthalpy 327 J/g, and water content 16 wt.%.

IC ICM C08B037-00
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 62, 63
ST **hyaluronic acid** ester **crosslinked** medical use; **amine crosslinked** tributylammonium hyaluronate prepn
IT Blood vessel
(artificial; **crosslinked hyaluronic acids** and medical uses thereof)
IT Organ, animal
(artificial; **crosslinked hyaluronic acids** and use as)
IT Drug delivery systems
(controlled-release; **crosslinked hyaluronic acids** and medical uses thereof)
IT Cosmetics
Medical goods
(**crosslinked hyaluronic acids** and medical uses thereof)
IT Prosthetic materials and Prosthetics
Synovial fluid
(**crosslinked hyaluronic acids** and use as)
IT Prosthetic materials and Prosthetics
(implants; **crosslinked hyaluronic acids** and use as)

IT Drug delivery systems
(ophthalmic; **crosslinked hyaluronic acids** and use as)
IT Drug delivery systems
(solns., ear; **crosslinked hyaluronic acids** and use as)
IT Eye
(vitreous humor; **crosslinked hyaluronic acids** and use as)
IT 267882-31-5
RL: NUU (Other use, unclassified); USES (Uses)
(activator; for **crosslinking hyaluronic acids** for medical uses)
IT **267882-30-4DP**, sulfated **267882-30-4P 267882-32-6P 267882-33-7P 267882-34-8P**
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**crosslinked hyaluronic acids** and medical uses thereof)
IT **267882-30-4DP**, sulfated **267882-30-4P 267882-32-6P 267882-33-7P 267882-34-8P**
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**crosslinked hyaluronic acids** and medical uses thereof)
RN 267882-30-4 HCAPLUS
CN Hyaluronic acid, ion( neg.), N,N,N-tributyl-1-butanaminium, polymer with 1,3-propanediamine (9CI) (CA INDEX NAME)

CM 1

CRN 109-76-2
CMF C3 H10 N2



CM 2

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

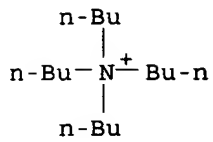
CM 3

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

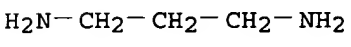
CRN 10549-76-5
CMF C16 H36 N



RN 267882-30-4 HCAPLUS
CN Hyaluronic acid, ion( neg.), N,N,N-tributyl-1-butanaminium, polymer with 1,3-propanediamine (9CI) (CA INDEX NAME)

CM 1

CRN 109-76-2
CMF C3 H10 N2



CM 2

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

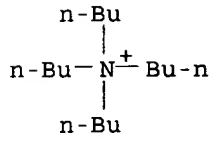
CM 3

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

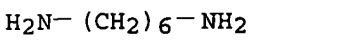
CRN 10549-76-5
CMF C16 H36 N



RN 267882-32-6 HCAPLUS
CN Hyaluronic acid, ion (neg.), N,N,N-tributyl-1-butanaminium, polymer with 1,6-hexanediamine (9CI) (CA INDEX NAME)

CM 1

CRN 124-09-4
CMF C6 H16 N2



CM 2

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

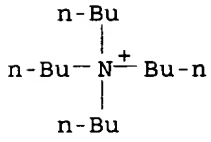
CM 3

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

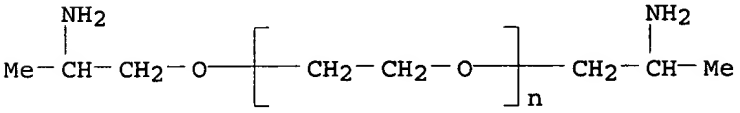
CRN 10549-76-5
CMF C16 H36 N



RN 267882-33-7 HCAPLUS
CN Hyaluronic acid, ion (neg.), N,N,N-tributyl-1-butanaminium, polymer with .alpha.-(2-aminopropyl)-.omega.-(2-aminopropoxy)poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM 1

CRN 70939-81-0
CMF (C2 H4 O)n C6 H16 N2 O
CCI PMS



CM 2

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

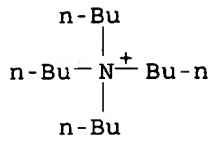
CM 3

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

CRN 10549-76-5
CMF C16 H36 N



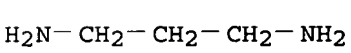
RN 267882-34-8 HCAPLUS
CN Hyaluronic acid, ion (neg.), N,N,N-tributyl-1-butanaminium, polymer with 1,3-propanediamine, copper salt (9CI) (CA INDEX NAME)

CM 1

CRN 267882-30-4
CMF (C16 H36 N . C3 H10 N2 . x Unspecified)x
CCI PMS

CM 2

CRN 109-76-2
CMF C3 H10 N2



CM 3

CRN 111677-24-8
CMF C16 H36 N . x Unspecified

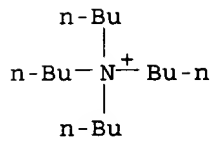
CM 4

CRN 54597-23-8
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 5

CRN 10549-76-5
CMF C16 H36 N



L30 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:335447 HCAPLUS
DOCUMENT NUMBER: 132:323187
TITLE: Preparation of crosslinked carboxy-containing polysaccharides having controlled crosslinking degree and high reproducibility
INVENTOR(S): Barbucci, Rolando; Sportoletti, Giancarlo
PATENT ASSIGNEE(S): Aquisitio S.p.A., Italy
SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000027886 | A1 | 20000518 | WO 1999-EP8480 | 19991109 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| IT 1303738 | B1 | 20010223 | IT 1998-MI2443 | 19981111 |
| IT 98MI2443 | A1 | 20000511 | | |
| BR 9915238 | A | 20010724 | BR 1999-15238 | 19991109 |
| EP 1137670 | A1 | 20011004 | EP 1999-971819 | 19991109 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002529549 | T2 | 20020910 | JP 2000-581063 | 19991109 |
| NO 2001002316 | A | 20010706 | NO 2001-2316 | 20010510 |

PRIORITY APPLN. INFO.: IT 1998-MI2443 A 19981111
WO 1999-EP8480 W 19991109

OTHER SOURCE(S): MARPAT 132:323187

AB The crosslinked carboxy-contg. polysaccharides, useful for medical, pharmaceutical and cosmetic fields, is prepd. by activating carboxy groups of a polysaccharide (e.g., CM-cellulose tetrabutylammonium salt) in anhyd. aprotic solvent (e.g., DMF) and then the reacting the activated polysaccharide with a **polyamine** (e.g., 1,3-diaminopropane). The crosslinked polysaccharide may be subjected to sulfation of the five hydroxy groups.

IC ICM C08B015-00
ICS C08B037-04; C08B037-08

CC 43-3 (Cellulose, Lignin, Paper, and Other Wood Products)
Section cross-reference(s): 62, 63

IT 9003-01-4, Polyacrylic acid 9004-32-4, CM-cellulose **9004-61-9**, **Hyaluronic acid** 9005-49-6, Heparin, reactions 9007-28-7, Chondroitin sulfate 9012-76-4, Chitosan 9032-53-5, Cellulosic acid 9050-30-0, Heparan sulfate 9057-06-1, Carboxymethylstarch 9067-32-7, **Hyaluronic acid**, sodium salt 24967-94-0, Dermatan sulfate 72270-19-0, Carboxymethyl glucan 102199-00-8 111677-24-8 119495-91-9 152842-67-6 267239-76-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of **crosslinked** carboxy-contg. polysaccharides having controlled **crosslinking** degree and high reproducibility)

IT **9004-61-9**, **Hyaluronic acid**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of **crosslinked** carboxy-contg. polysaccharides having controlled **crosslinking** degree and high reproducibility)

RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:105910 HCAPLUS
DOCUMENT NUMBER: 128:169784
TITLE: Solid polymer electrolyte batteries
INVENTOR(S): Takei, Fumio; Takahashi, Toru; Yoshida, Hiroaki
PATENT ASSIGNEE(S): Fujitsu Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

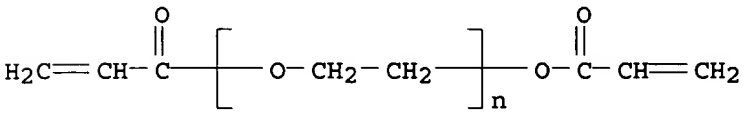
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 10040957 | A2 | 19980213 | JP 1996-196425 | 19960725 |

AB The batteries have a cathode and an anode holding a solid polymer electrolyte having a polymer matrix contg. a backbone of polysaccharides or their derivs. The backbone is selected from glucan, galactan, alginic acid, fructan, chondroitin sulfate, hyaluronic acid, mannan, and chitin; and the polymer may have functional group side chain attached to the backbone.

IC ICM H01M010-40
ICS H01M010-40; C08B037-00; C08L005-00; H01M006-18
CC 52-2 (Electrochemical, Radiational, and Thermal Energy Technology)
IT 108-32-7P, Propylene carbonate 14283-07-9P, Lithium fluoroborate 202934-96-1P 202934-98-3P 202935-00-0P 202935-02-2P 202935-04-4P **202935-06-6P** 202935-08-8P 202935-10-2P
RL: DEV (Device component use); IMF (Industrial manufacture); PREP (Preparation); USES (Uses)
(compns. and manuf. of solid polymer electrolyte with polysaccharide matrixes for batteries)
IT **202935-06-6P**
RL: DEV (Device component use); IMF (Industrial manufacture); PREP (Preparation); USES (Uses)
(compns. and manuf. of solid polymer electrolyte with polysaccharide matrixes for batteries)
RN 202935-06-6 HCAPLUS
CN Hyaluronic acid, 2-propenoate, carboxymethyl ether, polymer with .alpha.-(1-oxo-2-propenyl)-.omega.-[(1-oxo-2-propenyl)oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM 1

CRN 26570-48-9
CMF (C2 H4 O)n C6 H6 O3
CCI PMS



CM 2

CRN 202935-05-5
CMF C3 H4 O2 . x C2 H4 O3 . x Unspecified

CM 3

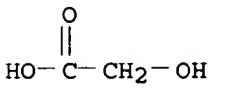
CRN 9004-61-9

CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

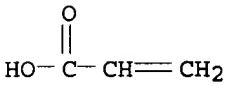
CM 4

CRN 79-14-1
CMF C2 H4 O3



CM 5

CRN 79-10-7
CMF C3 H4 O2



L30 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:302811 HCAPLUS
DOCUMENT NUMBER: 126:279255
TITLE: Physiologically compatible and water-insoluble hydrazine or hydrazide compound-crosslinked hyaluronic acid gels and their manufacture
INVENTOR(S): Kyota, Juko; Ueno, Norio
PATENT ASSIGNEE(S): Shiseido Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 09059303 | A2 | 19970304 | JP 1995-234598 | 19950822 |

AB The title gels useful for making contact lenses, prosthetic parts, etc. (no data), are condensation crosslinked with specified di(or bi)hydrazine and di(or bi)hydrazide compds. Thus, a crosslinked product was prepd. by using 1,4-dihydrazinophthalazine as crosslinker and a hyaluronic acid.
IC ICM C08B037-08
ICS A61L027-00; A61L031-00
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 63
IT **188968-15-2P**, Hyaluronic acid-1,4-dihydrazinophthalazine copolymer
**188968-25-4P**, Adipic dihydrazide-hyaluronic acid copolymer
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(physiol. compatible and water-insol. hydrazine or hydrazide compd.-crosslinked hyaluronic acid gels and manuf.)
IT **188968-15-2P**, Hyaluronic acid-1,4-dihydrazinophthalazine copolymer
**188968-25-4P**, Adipic dihydrazide-hyaluronic acid copolymer

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(physiol. compatible and water-insol. hydrazine or hydrazide compd.-crosslinked hyaluronic acid gels and manuf.)

RN 188968-15-2 HCAPLUS
CN Hyaluronic acid, polymer with 2,3-dihydro-1,4-phthalazinedione dihydrazone (9CI) (CA INDEX NAME)

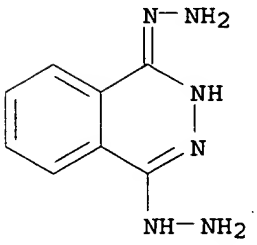
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 484-23-1
CMF C8 H10 N6



RN 188968-25-4 HCAPLUS
CN Hyaluronic acid, polymer with hexanedioic acid dihydrazide (9CI) (CA INDEX NAME)

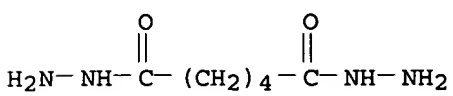
CM 1

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 1071-93-8
CMF C6 H14 N4 O2



L30 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:696062 HCAPLUS
DOCUMENT NUMBER: 123:86466
TITLE: Manufacture of physiologically compatible crosslinked hyaluronic acids and its mixture
INVENTOR(S): Ikada, Yoshito; Tabata, Yasuhiko; Oka, Takashige;

Tomihata, Kenji
PATENT ASSIGNEE(S): Gunze Kk, Japan; Kaken Pharma Co Ltd
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

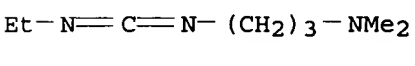
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 07102002 | A2 | 19950418 | JP 1993-245072 | 19930930 |

AB Crosslinked hyaluronic acids with low soly. in water and useful as viscoelastic materials or gels for treatment of eye illness and arthritic joint are manufd. by crosslinking a hyaluronic acid with carbodiimide, e.g. 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and optionally other diamine group-contg. amino acids or their esters and polyepoxy compds.

IC ICM C08B037-08
ICS A61K047-36
ICA A61K009-00
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 63
IT 164466-33-5P **165324-65-2P 165324-66-3P**
**165324-67-4P**
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(manuf. of physiol. compatible crosslinked hyaluronic acids and mixt.)
IT **165324-65-2P 165324-66-3P 165324-67-4P**
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(manuf. of physiol. compatible crosslinked hyaluronic acids and mixt.)
RN 165324-65-2 HCAPLUS
CN Hyaluronic acid, polymer with N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride (9CI) (CA INDEX NAME)

CM 1

CRN 25952-53-8
CMF C8 H17 N3 . Cl H



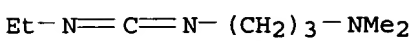
CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 165324-66-3 HCAPLUS
CN L-Lysine, methyl ester, polymer with N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride and hyaluronic acid (9CI) (CA INDEX NAME)

CM 1

CRN 25952-53-8
CMF C8 H17 N3 . Cl H



● HCl

CM 2

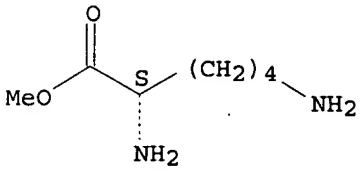
CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 687-64-9
CMF C7 H16 N2 O2

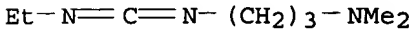
Absolute stereochemistry.



RN 165324-67-4 HCAPLUS
CN L-Lysine, polymer with N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride and hyaluronic acid (9CI) (CA INDEX NAME)

CM 1

CRN 25952-53-8
CMF C8 H17 N3 . Cl H



● HCl

CM 2

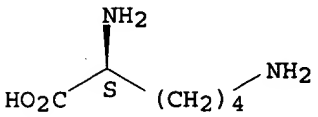
CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.



L30 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:137558 HCAPLUS
DOCUMENT NUMBER: 120:137558
TITLE: Photocurable glycosaminoglycan derivatives, crosslinked glycosaminoglycans and method of production thereof
INVENTOR(S): Matsuda, Takehisa; Moghaddan, Minoo J.; Sakurai, Katsukiyo
PATENT ASSIGNEE(S): Seikagaku Kogyo K. K., Japan
SOURCE: Eur. Pat. Appl., 55 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 554898 | A2 | 19930811 | EP 1993-101838 | 19930205 |
| EP 554898 | A3 | 19940126 | | |
| EP 554898 | B1 | 19970507 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 06073102 | A2 | 19940315 | JP 1992-355441 | 19921221 |
| JP 2855307 | B2 | 19990210 | | |
| RU 2139886 | C1 | 19991020 | RU 1993-4491 | 19930203 |
| CA 2088831 | AA | 19930806 | CA 1993-2088831 | 19930204 |
| HU 71625 | A2 | 19960129 | HU 1993-297 | 19930204 |
| HU 215503 | B | 19990128 | | |
| AU 9332878 | A1 | 19930812 | AU 1993-32878 | 19930205 |
| AU 670921 | B2 | 19960808 | | |
| CN 1075970 | A | 19930908 | CN 1993-102682 | 19930205 |
| CN 1083455 | B | 20020424 | | |
| US 5462976 | A | 19951031 | US 1993-13799 | 19930205 |
| AT 152736 | E | 19970515 | AT 1993-101838 | 19930205 |
| ES 2102537 | T3 | 19970801 | ES 1993-101838 | 19930205 |
| US 5763504 | A | 19980609 | US 1995-476236 | 19950607 |

PRIORITY APPLN. INFO.:
JP 1992-47744 A 19920205
JP 1992-203209 A 19920708
JP 1992-355441 A 19921221
US 1993-13799 B3 19930205

AB The title biopolymers with good physiol. compatibility and biol. degradability, useful for medical (e.g., prosthetic moldings) or pharmaceutical use (e.g., for drug slow-release coating), are prepd. based on modification of functional groups of substrates via, e.g., ester and amide linkages, using photosensitive modifiers which can be cured by free-radical mechanism. Example of a title deriv. was the cinnamate ester of hyaluronic acid which was formed by using cinnamoyl chloride in esterification; and the DMF soln.-cast film of the ester could be cured by

UV light.
IC ICM C08B037-10
ICS C08B037-08; A61L027-00; A61K047-48
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 63
IT 152787-14-9 152787-17-2 153369-05-2 **153369-06-3**
RL: USES (Uses)
(photoprepn. of crosslinked biodegradable biocompatible, for medical use)
IT **153369-06-3**
RL: USES (Uses)
(photoprepn. of crosslinked biodegradable biocompatible, for medical use)
RN 153369-06-3 HCAPLUS
CN Hyaluronic acid, 3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinepropanoate (ester), homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 153130-77-9
CMF C8 H10 N2 O4 . x Unspecified

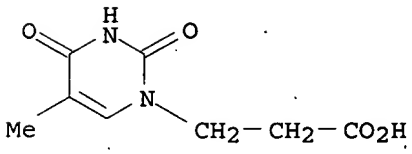
CM 2

CRN 9004-61-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 6214-59-1
CMF C8 H10 N2 O4




L30 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:656535 HCAPLUS
DOCUMENT NUMBER: 119:256535
TITLE: Photopolymerizable biodegradable hydrogels as tissue contacting material and controlled-release carriers
INVENTOR(S): Hubbell, Jeffrey A.; Pathak, Chandrashekhar P.; Sawhney, Amarpreet S.; Desai, Neil P.; Hill, Jennifer L.
PATENT ASSIGNEE(S): University of Texas System, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9317669 | A1 | 19930916 | WO 1993-US1773 | 19930301 |

W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

| | | | | | |
|---|---|---|---|---|---|
| AU 9337353 | A1 | 19931005 | AU 1993-37353 | 19930301 | |
| AU 673160 | B2 | 19961031 | | | |
| EP 627911 | A1 | 19941214 | EP 1993-906255 | 19930301 | |
| EP 627911 | B1 | 20001025 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| JP 07507056 | T2 | 19950803 | JP 1993-515790 | 19930301 | |
| JP 3011768 | B2 | 20000221 | | | |
| BR 9306038 | A | 19980113 | BR 1993-6038 | 19930301 | |
| CA 2117588 | C | 19980825 | CA 1993-2117588 | 19930301 | |
| AT 197125 | E | 20001115 | AT 1993-906255 | 19930301 | |
| ES 2153378 | T3 | 20010301 | ES 1993-906255 | 19930301 | |
| PRIORITY APPLN. INFO.: | | | US 1992-843485 | A 19920228 | |
| | | | WO 1993-US1773 | A 19930301 | |

AB Hydrogenls of polymd. and crosslinked macromers comprising hydrophilic oligomers having biodegradable monomeric or oligomeric extensions, which are terminated on free ends with end cap monomers or oligomers capable of polymn. and crosslinking are described. Biodegrdn. occurs at the linkage within the extension oligomers and results in fragments which are non-toxic and easily removed from the body. Lysozyme was added to a soln. of PEG-dL-lactic acid-diacrylate monomer to obtain a 24% monomer soln. and was then polymd. in presence of an initiator by UV light. Lysozyme was released from the above gel over an 8 day interval with the max. rate within the 1st 2 days. The hydrogels are used for prevention of adhesion formation after surgical procedures, controlled release of drugs, temporary protection or sepn. of tissue surfaces, adhering of sealing tissues together, and preventing the attachment of cells to tissue surface.

IC ICM A61K009-50

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 38

IT 1648-99-3D, Tresyl chloride, reaction products with PEG monoacrylate and albumin 26403-58-7D, reaction products with tresyl chloride and albumin 146584-44-3 146584-48-7 146584-49-8 151205-67-3 **151205-68-4** 151205-69-5D, reaction products with isocyanoethyl methacrylate
RL: BIOL (Biological study)
(hydrogels comprising, photopolymerizable and biodegradable)

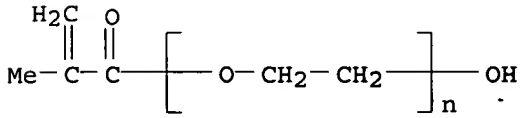
IT **151205-68-4**
RL: BIOL (Biological study)
(hydrogels comprising, photopolymerizable and biodegradable)

RN 151205-68-4 HCAPLUS

CN Hyaluronic acid, polymer with .alpha.-(2-methyl-1-oxo-2-propenyl)-.omega.-hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM 1

CRN 25736-86-1
CMF (C2 H4 O)n C4 H6 O2
CCI PMS



CM 2

CRN 9004-61-9

CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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FILE LAST UPDATED: 26 SEP 2002              <20020926/UP>
MOST RECENT DERWENT UPDATE            200262   <200262/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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    enabled in WPINDEX/WPIDS and WPIX  >>>

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               DEL HIS Y

     FILE 'WPIDS' ENTERED AT 10:21:32 ON 30 SEP 2002
L1          1920 S HYALURONIC ACID#
L2         16782 S POLYAMINE# OR POLY (3W) AMINE#
L3         86236 S CROSSLINK? OR CROSS LINK?
L4             8 S L1 (L) L2
L5             6 S L1 AND L2 AND L3
L6             9 S L1 AND L2
L7           281 S L1 (L)  L3
L8            27 S L1 (L) AMINE# (L) L3
L9            34 S L8 OR L4 OR L5 OR L6

     FILE 'WPIDS' ENTERED AT 10:27:04 ON 30 SEP 2002

=> d que L9
L1          1920 SEA FILE=WPIDS ABB=ON  PLU=ON  HYALURONIC ACID#
L2         16782 SEA FILE=WPIDS ABB=ON  PLU=ON  POLYAMINE# OR POLY (3W) AMINE#
L3         86236 SEA FILE=WPIDS ABB=ON  PLU=ON  CROSSLINK? OR CROSS LINK?
L4             8 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (L) L2
L5             6 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 AND L2 AND L3
L6             9 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 AND L2
L8            27 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (L) AMINE# (L) L3
L9            34 SEA FILE=WPIDS ABB=ON  PLU=ON  L8 OR L4 OR L5 OR L6


=> d .wp tech 1-34

L9   ANSWER 1 OF 34  WPIDS (C) 2002 THOMSON DERWENT
AN   2002-566534 [60]    WPIDS
DNN  N2002-448532        DNC C2002-160505
TI   Restoring damaged or degenerated intervertebral disc comprises
     percutaneous injection of  in situ setting formulation.
DC   A96 B04 D22 P34
IN   BERRADA, M; CHAPUT, C; CHENITE, A; DESROSIERS, E A
```

PA (BIOS-N) BIO SYNTECH CANADA INC
CYC 99
PI WO 2002040070 A2 20020523 (200260)* EN 46p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
AU 2002021370 A 20020527 (200261)
ADT WO 2002040070 A2 WO 2001-CA1623 20011115; AU 2002021370 A AU 2002-21370 20011115
FDT AU 2002021370 A Based on WO 200240070
PRAI US 2000-248568P 20001116; US 2000-248226P 20001115
AB WO 200240070 A UPAB: 20020919
NOVELTY - Restoring a damaged or degenerated intervertebral disc involves administering percutaneously an injectable in situ setting formulation (A) in the nucleus pulposus of the disc for increasing the thickness of the damaged or degenerated disc. The formulation becomes viscous, pasty or turns into a gel or solid in situ within the disc and is retained within the annulus fibrosus of the disc.

USE - For restoring a damaged or degenerated intervertebral disk (claimed).

ADVANTAGE - The formulations decompress the injected intervertebral disc and stabilize the spine of the patient. Hence the restoration of damaged or degenerated intervertebral disk provides a more biomechanically stable spine. The formulations are flowable and have a viscosity above 10 mPa.s at the time of administration.

Dwg.0/7

TECH UPTX: 20020919
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: (A) once administered mixes and combines in situ nucleus matters and host cells or biochemicals and living matters.
Preferred Formulation: (A) further comprises at least one bioactive agent or pharmaceutical agent or drug selected from a cell stimulant, a cell preservative or a cell differentiation factor (preferably cytokine or growth factor, or anti-pain or anti-inflammation drug).
TECHNOLOGY FOCUS - POLYMERS - Preferred Formulation: (A) forms a viscous, gel, pasty or solid material in situ. The gel is a self-gelling or thermogelling solution selected from cellulosic, polysaccharide and/or polypeptide aqueous solution. (A) comprises a polymeric aqueous solution covalently **crosslinkable** into an aqueous gel in situ. The thermogelling aqueous solution comprises chitosan and a phosphate salt. (A) contains chondroitin sulfate, **hyaluronic acid** or poly(ethylene glycol) or their derivatives. (A) comprises (wt.%)
(I) a formulation containing a component (0.1 - 5) selected from water soluble cellulosic, polysaccharide or polypeptidic and/or their derivatives, a component (C) (1 - 20) selected from polyol salt or sugar, and a salt (S1) (1 - 20) selected from phosphate, carbonate, sulfate or sulfonate, or
(II) a formulation containing chitosan or collagen and/or their derivatives (0.1 - 5, preferably 0.1 - 3), (C) (1 - 20) and optionally a water-soluble chemically reactive organic compound (0.01 - 10, preferably 0.01 - 5) or
(III) a formulation containing a water soluble polymer (P1) (0.1 - 5) selected from cellulosic, polysaccharide or polypeptidic and a water-soluble salt (S) (1 - 20, preferably 1 - 10) selected from phosphate, glycerol-phosphate, glucose-phosphate or fructose phosphate.
In all the formulations, (A) has a pH of 6.5 - 7.4 and turns into a gel within 20 - 70 (preferably 20 - 40)degreesC, which has a physiologically acceptable consistency for increasing the thickness of the disc and provides a mechanical support once injected in the disc. When the organic compound is present in (A), (A) gels at 4 - 70degreesC. (A) comprises

methyl-cellulose, hydroxyethyl-cellulose and/or hydroxypropyl-methylcellulose, and a biocompatible physiologically safe polymer, which is polymerized or covalently **crosslinked** after being injected in situ. (A) further comprises a nonsoluble particulate material (preferably a biodegradable organic particulate material made of an absorbable polymer, gelatin, or collagen).
Preferred Components: The polyol is histidinol, acetol, diethylstilbestrol, indole-glycerol, sorbitol, ribitol, xylitol, arabinitol, erythritol, inositol, mannitol, glucitol, palmitoyl-glycerol, linoleolyl-glycerol, oleoyl-glycerol and/or arachidonoyl-glycerol. (C) is methyl-cellulose, hydroxyethyl-cellulose, hydroxypropyl-(methyl)cellulose, chitosan and/or collagen. The absorbable polymer is poly(lactic acid), poly(glycolic acid), poly(lactic-co-glycolic), poly(lactone), poly(orthoester), poly(anhydride) or poly(carbonate). (P1) is methyl-cellulose, hydroxyethyl-cellulose, hydroxypropyl-cellulose, hydroxypropyl methylcellulose, chitosan and/or collagen.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: (S1) is a mono-phosphate dibasic salt of glycerol selected from glycerol-2-phosphate, sn-glycerol 3-phosphate or L-glycerol-3-phosphate salt. The sugar is a mono-phosphate dibasic salt, mono-sulfate salt or a mono-carboxylic acid salt of polyol or sugar (preferably fructose, galactose, ribose, glucose, xylose, rhamnulose, sorbose, erythrulose, deoxy-ribose, ketose, mannose, arabinose, fuculose, fructopyranose, ketoglucose, sedoheptulose, trehalose, tagatose, sucrose, allose, threose, xylulose, hexose, methylthio-ribose and/or methylthio-deoxy-ribulose).
Preferred Formulation: (A) comprises chitosan-beta-glycerophosphate, chitosan-alpha-glycerophosphate, chitosan-glucose-1-glycero-phosphate and chitosan-fructose-6-glycerolphosphate, an organic solvent, at least one fatty acid, a metabolically absorbable solvent. The fatty acid is oleate, palmitate, myristate, stearate, palmitoleate or vaccenate or their derivatives. The fatty acid is mixed with a metabolically absorbable solvent or liquid vehicle to reduce viscosity and allow injectability. The absorbable solvent is water, triacetin, alcohol, glycerol or a lactate-based solvent. The water-soluble chemically reactive organic compound is reactive toward free **amine** groups and is a functionalized poly(ethylene glycol) (preferably monofunctional methoxy-poly(ethylene glycol) or multifunctional poly(ethylenen glycol), aldehyde, anhydride acid, azide, azolide, carboimide, carboxylic acid, epoxide, ester, glycidyl ether, halide, imidazole, imidate, succinimide, succinimidyl ester and/or (meth)acrylate. (A) is a dispersion comprising a non-soluble solid component selected from microparticles, microbeads, microspheres or granules.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Formulation: (A) comprises living tissue cells, which are adhered onto a solid substrate prior to administration. (A) further comprises cells (preferably autologous or modified stem cells or chondrocytes).
Preferred Method: The nucleus pulposus is excised prior to administering (A).
TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Formulation: (A) further comprises an inorganic or mineral particulate material selected from bioglass, calcium phosphate or calcium carbonate. (I) and (II) comprise a mono-phosphate dibasic salt or a glycerophosphate salt.
Preferred Components: (S) is a dibasic phosphate salt selected from sodium or magnesium salt (preferably sodium phosphate or magnesium phosphate).

L9 ANSWER 2 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-556018 [59] WPIDS
DNC C2002-157602
TI Sulfation of uronic acid-containing polysaccharide such as dermatan or heparin sulfate involves converting polysaccharide to its amine salt, treating salt with sulfuric acid, adjusting pH and treating with sulfating

agent.
DC A11 A32 E19
IN CONRAD, E H; GUO, S Y C
PA (VASC-N) VASCULAR THERAPEUTICS INC
CYC 1
PI US 6388060 B1 20020514 (200259)* 8p
ADT US 6388060 B1 Provisional US 1998-107396P 19981106, US 1999-433879 19991104
PRAI US 1998-107396P 19981106; US 1999-433879 19991104
AB US 6388060 B UPAB: 20020916
NOVELTY - A uronic acid-containing polysaccharide is converted to its **amine** salt. The **amine** salt is dissolved in an aprotic solvent and treated with sulfuric acid. N,N'-carbodiimide is added and the pH of the solution is adjusted to above 12 for 30-60 minutes and then to 7. A sulfating agent is contacted with the solution to form a sulfated uronic acid-containing polysaccharide.
USE - Sulfating uronic acid-containing polysaccharides such as dermatan sulfate, heparin, chondroitin sulfate, heparin sulfate, alginic acid and **hyaluronic acid**.
ADVANTAGE - The method minimizes modifications of carboxyl group while maximizing the degree of sulfation up to 4 sulfates per disaccharide. The carbodiimide or sulfate derivatives of carboxylic acid formed during the reaction are converted back to original carboxylic acids, hence degradation or **cross-linking** of polysaccharide during the reaction is eliminated.
Dwg.0/0
TECH UPTX: 20020916
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Amine Salt: The amine salt is a quaternary or tertiary amine salt.
Preferred Process: The amine salt of uronic acid-containing polysaccharide is treated with sulfuric acid at 10-35 degreesC for 1-3 hours. The sulfating agent is contacted with the reaction solution at 50-60 degreesC. The ratio of sulfating agent to uronic acid-containing polysaccharide is 1:0.5-1:2. Heparin is sulfated by maintaining sulfation reaction for 1-3 hours. The reaction solution, after treating with sulfuric acid, is treated with base in an aqueous solution at a pH of above 12 for 30-60 minutes and then to pH 7. The sulfuric acid is present in 1-25 fold weight excess over polysaccharide. N,N'-carbodiimide is present in equimolar ratio to sulfuric acid.

L9 ANSWER 3 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-519057 [55] WPIDS
DNN N2002-410923 DNC C2002-146734
TI New biodegradable, blood-compatible biopolymer comprising **crosslinked** polyubiquitin, forming hydrogels or matrices useful e.g. as wound dressings, drug delivery vehicles or enzyme biosensors.
DC A96 B04 P34
IN BOSSE, M
PA (VIRI-N) VIRIDIS BIOTECH INC
CYC 96
PI WO 2001091814 A2 20011206 (200255)* EN 75p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001067181 A 20011211 (200255)
ADT WO 2001091814 A2 WO 2001-CA784 20010529; AU 2001067181 A AU 2001-67181 20010529
FDT AU 2001067181 A Based on WO 200191814
PRAI US 2000-207325P 20000530
AB WO 200191814 A UPAB: 20020829

NOVELTY - A novel biopolymer (A) comprises a 3-dimensionally **crosslinked** mixture of ubiquitin (I) (a small protein having a sequence of 76 amino acids given in the specification) and at least one **crosslinking** agent (II).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) preparation of (A);

(ii) a biopolymer comprising (I), a solvent for (I) and at least one (II); and

(iii) the use of (I) in the preparation of (A).

ACTIVITY - Hemostatic; vulnerary.

MECHANISM OF ACTION - None given in the source material.

USE - (A) form hydrogels or matrices useful as wound dressings, biodegradable vehicles for oral, parenteral or topical drug delivery, enzyme biosensors for detection of nucleic or peptide molecules, in situ hybridization systems (e.g. for use in diagnostic assays), in vitro model systems for research, hemostatic agents, prostheses or implants (possibly containing cell cultures).

ADVANTAGE - (A) are biodegraded to non-toxic, endogenous materials; have good blood compatibility and low immunogenicity and can be prepared with a wide range of controllable properties (e.g. hydrophilicity, charge, degree of **crosslinking**, drug uptake and degradation/release kinetics).

Dwg.0/18

TECH UPTX: 20020829

TECHNOLOGY FOCUS - POLYMERS - Preferred Ubiquitins: (I) contains at least one ubiquitin unit or ubiquitin units in tandem, preferably 2-25 (especially 7) ubiquitin units. The ubiquitins may be recombinant or naturally occurring ubiquitins, or their mutants, analogs, fragments or derivatives.

Preferred **Crosslinking** Agents: (II) is a photoreactive or thermoreactive **crosslinking** agent specifically containing carboxy (or derivative, e.g. ester, halide, azide or hydrazide), sulfonic acid derivative, semicarbazide, thiosemicarbazide, aldehyde, ketone, alcohol, chloride, bromide, iodide, thio, primary, secondary or tertiary **amine**, hydrazide, epoxide or maleimide reactive groups. Preferably (II) is selected from polyethylene glycols or their derivatives (most preferred), **polyamines**, **amines**, polyvinyl compounds, polystyrene, epoxy compounds, silicones, proteins (specifically keratin, collagen, elastin, actin, myosin, fibrinogen, silk or gelatin), polysaccharides (specifically cellulose, amylose, **hyaluronic acid**, chitin, chitosan, xylan or mannan), silica, p-azidobenzoyl hydrazide, N-5-azido-2-nitrobenzoyloxy-succinimide, disuccinimidyl glutamate, dimethyl pimelimidate dihydrochloride, dimethyl suberimidate dihydrochloride, dithio-bis-(succinimidyl propionate), disuccinimidyl suberate, bis-(sulfosuccinimidyl suberate), 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride, isocyanates, aldehydes (specifically glutaraldehyde or paraformaldehyde) or their derivatives, In particular (II) is a polyethylene glycol derivative of formula X-(CH2CH2O)n-X (II'), especially an activated bifunctionalized polyethylene oxide.

n = at least 1;

X = covalent bond, group capable of reacting with an amino acid, R or OR (with the O bonded to the polyethylene oxide); and

R = methylene, ethylene, propylene, phenylene or phenylene carbamate (optionally substituted by at least one alkyl, aryl, halo, NO2, oxo, COOH, OH, thio, sulfonate or phosphate groups).

Preparation: Claimed preparation of (A) involves mixing a solution of (I) with at least one (II) and inducing polymerization for sufficient time to cause **crosslinking**.

L9 ANSWER 4 OF 34 WPIDS (C) 2002 THOMSON DERWENT

AN 2002-507899 [54] WPIDS

DNC C2002-144365

TI Manufacture of amide derivatives of hyaluronic acid for correction of facial wrinkles, involves cross-linking polymer or oligomer having amino groups with hyaluronic acid or its salts using carboxyl activating agent.
DC A11 A25 A96 D21 D22 E19
IN HAN, K; KIM, J; LEE, J; MOON, T
PA (GLDS) LG CHEM INVESTMENT LTD
CYC 96
PI WO 2002030990 A1 20020418 (200254)* EN 29p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001094320 A 20020422 (200254)
ADT WO 2002030990 A1 WO 2001-KR1687 20011010; AU 2001094320 A AU 2001-94320 20011010
FDT AU 2001094320 A Based on WO 200230990
PRAI KR 2000-59443 20001010
AB WO 200230990 A UPAB: 20020823
NOVELTY - A polymer or oligomer having at least two **amine** groups is **cross-linked** with **hyaluronic acid** or its hyaluronate salts through amidation reaction under existence of carboxyl group activating agent.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for **cross-linked** amide derivative of **hyaluronic acid**.
USE - For manufacturing amide derivative of **hyaluronic acid** used for prevention of adhesion after surgical operation, correction of facial wrinkles, dermal augmentation, tissue engineering and osteoarthritic viscosupplement.
ADVANTAGE - The **cross-linked** amide derivatives of **hyaluronic acid** has high viscoelasticity, and characteristics of sponge or rubber. The **cross-linking** reaction of the polymer and **hyaluronic acid** by amidation is performed easily without using toxic organic solvent, at a faster reaction rate to form amide derivative of **hyaluronic acid** in a higher yield.
DESCRIPTION OF DRAWING(S) - The figure shows spectrum of infrared spectroscopy of the amide derivative of **hyaluronic acid** sample.
Dwg.4/5
TECH UPTX: 20020823
TECHNOLOGY FOCUS - POLYMERS - Preferred Process: The polymer or oligomer having amine group accepts proton so that positive charges under acidic or neutral condition by amidation reaction, is promoted using electrostatic attraction between the amine groups of polymer or oligomer and the carboxyl groups of hyaluronic acid or its salts.
The polymer or oligomer is polycationic polymer or oligomer charged positively by protonating the amine groups in the polymer. The hyaluronic acid or its salts has molecular weight of 10,000-10,000,000 and concentration of hyaluronic acid or its salt is 0.01-100 mg/ml. The ratio of the carboxyl groups of the hyaluronic acid or its salts to the amine groups of the polycationic polymer or oligomer is 1:0.01 to 100 in the reaction mixture.
0.0001-100 mg/ml of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride and 0-100 mg/ml of N-hydroxysuccinimide are added during amidation reaction.
Preferred Polymer: The polymer or oligomer is chitosan, chitosan derivatives, deacetylated hyaluronic acid, or its hyaluronate salts, deacetylated hyaluronic acid derivatives, deacetylated hyaluronate salt derivatives, polyethylene glycol or protein or peptide having two or more reactive amine groups which accepts proton.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Activating Agent: The carboxyl group activating agent is carbodiimide. The carbodiimide which is easily soluble in water, is selected from 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC), 1-alkyl-3-(3-dimethylaminopropyl) carbodiimides having structure similar to EDC, 1-ethyl-3-(3-(trimethylammonio) propyl carbodiimide (ETC) and 1-cyclohexyl-3-(2-morpholinoethyl) carbodiimide (CMC).
The compound such as N-hydroxysuccinimide (NHS), 1-hydoxybenzotriazole (HOBt), 3,4-dihydro-3-hydroxy-4-oxo-1,2,3-benzotriazine (HOOBt), 1-hydroxy-7-azabenzotriazole (HOAt) and N-hydroxysulfosuccinimide (sulfo-NHS), are added as auxiliary agent to amidation reaction.
Preferred Form: The amide derivative of hyaluronic acid is provided in the form of gel, membrane, bead or mesh.

L9 ANSWER 5 OF 34 WPIDS (C) 2002 THOMSON DERWENT.
AN 2002-489691 [52] WPIDS
DNN N2002-387161 DNC C2002-138965
TI Anastomosis stent for inserting into blood vessel, comprises two termini and primary lumen providing fluid passage between termini and is made of non-polyglycolic acid material that is resorbable in preset days.
DC A96 D22 P32 P34
IN CHU, G; DANILOFF, G Y; DELUSTRO, F A; FRANCO, K; DELUSTRO, F
PA (COHE-N) COHESION TECHNOLOGIES INC; (CHUG-I) CHU G; (DANI-I) DANILOFF G Y; (DELU-I) DELUSTRO F A; (FRAN-I) FRANCO K
CYC 95
PI WO 2002024114 A2 20020328 (200252)* EN 47p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001093109 A 20020402 (200252)
US 2002052572 A1 20020502 (200252)
ADT WO 2002024114 A2 WO 2001-US30085 20010925; AU 2001093109 A AU 2001-93109 20010925; US 2002052572 A1 Provisional US 2000-235036P 20000925, Provisional US 2001-259997P 20010105, US 2001-966800 20010925
FDT AU 2001093109 A Based on WO 200224114
PRAI US 2001-259997P 20010105; US 2000-235036P 20000925; US 2001-966800 20010925
AB WO 200224114 A UPAB: 20020815
NOVELTY - An anastomosis stent (100) for insertion into a lumen of vessel or tissue, comprises a first and second termini (106,108) having opening (102,104) at each end and a primary lumen (110) which provides fluid communication between openings of termini. The termini are sized to be inserted into the vessel. The stent is made of a non-polyglycolic acid material that is resorbable by the patient in about a few minutes up to about 90 days.

DETAILED DESCRIPTION - An anastomosis stent (100) for insertion into a lumen of vessel or tissue, comprises a first and a second termini (106,108) having opening (102,104) at each end and a primary lumen (110) which provides fluid communication between openings of termini. The termini are sized to be inserted into the vessel. The stent is made of a non-polyglycolic acid material that is resorbable by the patient in about a few minutes up to about 90 days.

INDEPENDENT CLAIMS are also included for: (i) A method of anastomosis which involves inserting the first terminus (FT) of the stent through an aperture into the cavity of a physiologically functioning vessel of a patient, and the second terminus (ST) of the stent into a conduit (200), such that an interface is formed between the vessel and the conduit about the aperture, and attaching the vessel to the conduit at the interface; (ii) A tissue plug for use in sealing an opening in a patient's tissue,

which comprises a solid object having a platen surface. The platen is adapted to cover the opening and contact the perimeter about the opening, or both. The solid object is comprised of a non-polyglycolic acid material that is resorbable by the patient in a maximum of about 90 days; and (iii) A method of sealing an opening in a patient's tissue which involves positioning the plug in relationship to an opening in a patient's tissue, such that the plug covers the opening, thereby forming an interface between the plug and the tissue. The patient's tissue is adhered to the plug to form a closure.

USE - For sealing an opening in the patient's tissue or blood vessel such as an artery, aorta, coronary artery or a vein of a patient during surgical techniques such as anastomosis (claimed). The stent and plug are used in endoscopic procedures performed in the abdomen or chest.

ADVANTAGE - The anastomosis stent provides mechanical support in surgical procedures such as anastomosis or to cover openings in tissue. The stent can be employed in an anastomosis involving any number of vessels of a patient including both arteries and vein. The stent can be constructed according to the particular vessel or tissue. The method also produces a sutureless anastomosis method.

DESCRIPTION OF DRAWING(S) - The figure shows an angled Y-shaped stent.

Stent 100

Openings 102,104

First and second terminus 106,108

Cylindrical portion 110

Conduit 200

Dwg.1A/4

TECH UPTX: 20020815

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Properties: The primary lumen is substantially straight, curved, or bent. The termini is tapered or shaped. A flange is present at first or second terminus. The termini have a diameter of 1-10 mm. The termini have different diameters. The termini are located 1-5 cm, preferably 2-3 cm apart. The stent further comprises a third terminus which has a fluid communication with the primary lumen through an intersecting lumen. The primary lumen and intersecting lumen intersect (non)perpendicularly. The material is resorbable in 7-10 days, preferably 1-2 days.

TECHNOLOGY FOCUS - POLYMERS - Preferred Material: The material comprises a frozen physiologic saline, or a hydrophilic compound. The hydrophilic compound comprises a polyethylene glycol-containing compound which is chemically conjugated with a naturally occurring compound such as protein. The protein is a collagenic material such as gelatin, type I, type II and/or type III collagens. The naturally occurring compound is a polysaccharide and glycosaminoglycan or a proteoglycan. The polysaccharide is **hyaluronic acid**, cyclodextrin, hydroxymethyl cellulose, cellulose ether and starch. The molecular weight of the polyethylene glycol is 100-20000 daltons. The hydrophilic material is a collagenic material containing a collagen that is chemically conjugated to a synthetic hydrophilic polymer. The hydrophilic polymer is polyethylene glycol or polyvinylpyrrolidone. The stent further comprises a tissue sealant on the surface. The sealant comprises polyethylene glycol such as polyethylene glycol di-succinimidyl glutarate, pentaerythritol polyethylene glycol ether tetra-succinimidyl glutarate, polyethylene glycol mono-succinimidyl succinate, polyethylene glycol mono-succinimidyl propionic acid, polyethylene glycol mono-succinimidyl succinamide, polyethylene glycol di-succinimidyl succinamide, polyethylene glycol di-epoxide, polyethylene glycol di-isocyanate, polyethylene glycol di-carbonyl diimidazole, pentaerythritol polyethylene glycol ether tetra-maleimido propionamide, pentaerythritol polyethylene glycol ether tetra-malimido propionate, polyethylene glycol di-**amine**, diglycero polyethylene glycol ether tetra-**amine**, pentaerythritol polyethylene glycol ether tetra-**amine**, polyethylene glycol

di-sulfhydryl, pentaerythritol polyethylene glycol ether tetra-sulfhydryl, pentaerythritol polyethylene glycol ether, diglycerol poly(ethylene glycol) ether and/or copolymers. Preferred Method: The vessel is attached to the bypass conduit at the interface, without need for a suture. A tissue sealant is introduced around or over the interface between the bypass conduit and the vessel, by injection or as a spray. The sealant is **cross-linked**. The sealant is made of collagenic material such as methylated collagen, atelopeptide collagen in solution and/or colony stimulating factors. The platen surface is supported by a pedestal structure having a pedestal lateral dimension. The surface is greater than or equal to the pedestal structure lateral dimension. The platen surface is non-polar which is shaped to conform to the human surface of the blood vessel. An additional tissue is placed and adhered in contact with the blood, such that the plug is interposed between the additional tissue and the tissue associated with the opening. Alternately, a sutureless method of anastomosis involves inserting the stent into lumen of physiologically functioning vessel and applying the tissue sealant at the interface to attach the conduit to the vessel such that the interface exhibits a tensile strength of at least about 1.3 N/cm2. The opening in a patient's tissue is alternately sealed by a sutureless method by positioning the plug with respect to the opening such that the plug contacts the perimeter about the opening, thereby forming an interface between the plug and tissue. Then the resorbable sealant is applied at the interface to form a closure.

L9 ANSWER 6 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-479503 [51] WPIDS
DNC C2002-136380
TI Formulation for treating ectoparasite such as headlice infection comprises a lower alcohol and a thickening agent.
DC A96 B05 C03
IN FREE, W L; GREIG, W V
PA (HAIR-N) HAIR ADVISORY CENT PTY LTD
CYC 97
PI WO 2002024182 A1 20020328 (200251)* EN 26p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001091485 A 20020402 (200252)
ADT WO 2002024182 A1 WO 2001-AU1183 20010920; AU 2001091485 A AU 2001-91485 20010920
FDT AU 2001091485 A Based on WO 200224182
PRAI AU 2000-280 20000921
AB WO 200224182 A UPAB: 20020812
NOVELTY - A treatment formulation for ectoparasites comprises (%w/w) a 1-4C lower alcohol (20 - 8, preferably 50 - 70), a thickening agent (0.1 - 20 preferably (1 - 5) and a vehicle.
ACTIVITY - Antiparasitic.
MECHANISM OF ACTION - None given
USE - As an ectoparasite formulation (claimed), for the treatment of headlice and other parasitic infections which are utilized in susceptible human and animal species.
ADVANTAGE - The formulation is effective in use and does not involve the use of toxic components. The lower alcohol evaporates oxothermally drawing heat from the body and providing cooling effect. The thickening agent promotes maximization of therapeutic action per dose, easy and safety of use in control dosage form, enhanced distribution across the treatment surfaces, has reduced flammability and has reduced risk of the potential of adverse eye contact.
Dwg.0/0

TECH UPTX: 20020812

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Formulation: The formulation further comprises (%w/w) a conditioning agent, anti-static agent, emulsion binding agent and/or stabilizing agent (0.05 - 20, preferably 0.1 - 5) and a thickening agent (1 - 5). The formulation comprises (%): lower alkanol (64), conditioning agent (0.2) and thickening agent (1). pH of the formulation is 4.5 - 8.5 (preferably 5.5 - 7.5). The formulation also comprises a secondary active component: (0.01 - 10, preferably 0.2 - 20, particularly 0.5 - 1)%. Preferred Components: The secondary active component is selected from essential oil (preferably tea tree oil or rosemary oil), or natural and synthetic pyrethroids or organophosphates. The carrier is water. The conditioning or anti-static agents are selected from cationic surfactant, anionic surfactant, **amines**, betaines, protein derivatives, amino acids or quaternary ammonium compounds (preferably quaternary ammonium compound). The emulsion stabilizer is selected from aluminum salts of long chain fatty acids, long chain fatty acids, 9-11C alcohols, 12-18C alcohols, 20-40C alcohols, 1-5C alkyl galactomannans, 18-38C alkyl hydroxystearoyl stearate, 14-30C glycols or lanolin (preferably 12-18C alcohol).

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The thickening agent is selected from linear, branched, **cross-linked**, naturally derived or synthetic polymers (preferably cellulose derivatives, or naturally derived polysaccharides or synthetic polymers; including polyethylene glycol, polyethylene oxide, polyvinyl pyrrolidone or polyacrylic acid); or acrylamide co-polymers, cross polymers or co-polymers having an acrylate component, alginic acid or alginates; carbomers, carboxymethyl polymers, betaines, tallow amides, stearamides, gums, cocamides, gelatins, kelp, polyethylene glycols, polymers containing polyethylene glycols, clay including bentonite; **hyaluronic acid**, lauramides, oleamides, palmamides or kernel amides (preferably carbomer, acrylamide co-polymers, or cross polymers or co-polymers containing an acrylate component). The conditioning or anti-static agent is selected from polyquaternium species, polyethylene glycol **amines**, polyethylene glycol amides, quaternium tallow **amines**, isostearamidopropyl compounds or stearamidopropyl compounds.

L9 ANSWER 7 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-329761 [36] WPIDS
DNN N2002-258810 DNC C2002-095325
TI New cross-linked derivative of partially N-deacetylated hyaluronic acid or its derivative useful in the preparation of e.g. biomaterial, pharmaceutical preparation.
DC A11 A96 B04 B07 D16 D22 P34
IN CRESCENZI, V; FRANCESCANGELI, A; RENIER, D
PA (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL
CYC 97
PI WO 2002018450 A1 20020307 (200236)* EN 28p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002013870 A 20020313 (200249)
ADT WO 2002018450 A1 WO 2001-EP10063 20010831; AU 2002013870 A AU 2002-13870 20010831
FDT AU 2002013870 A Based on WO 200218450
PRAI IT 2000-PD207 20000831
AB WO 200218450 A UPAB: 20020610
NOVELTY - New cross-linked derivative (a) of partially N-deacetylated hyaluronic acid or its derivative comprises at least one repeating unit.

DETAILED DESCRIPTION - New cross-linked derivative of partially N-deacetylated hyaluronic acid or its derivative comprises at least one repeating unit of formula (I).

R1 = H or optionally substituted 1-20C residue derived from an aldehyde of G;

R2 = optionally substituted G;

R = OH, O- or an alcoholic, or amino group of G;

G = aromatic, (aryl)aliphatic, cycloaliphatic or heterocyclic series;

R3 = H, SO3-, a residue or heavy metal salts of hemiesters of succinic acid;

R4 = COR or CH2OR3.

With the proviso that for R1 the aldehyde is liquid at room temperature.

INDEPENDENT CLAIMS are also included for the following:

(1) preparation of (a);

(2) a biomaterial comprising at least one (a) optionally in association with a natural, a (semi)synthetic polymer, or biologically or pharmacologically active substance (A);

(3) use of the biomaterial in association with (A) as vehicling agent for the preparation of slow release pharmaceutical compositions;

(4) a pharmaceutical composition comprising (a) as the active agent optionally in association with (A) and excipient and/or diluent; and

(5) use of (a) in association with radioactive and non-radioactive substances to be used in contrast systems, for the preparation of markers in vivo diagnostics for the identification and treatment of tumoral or damaged tissues.

USE - In the preparation of a biomaterial, which is useful as a healthcare or surgical article selected from microspheres, nanospheres, membranes, sponges, threads, films, gauzes, guide channel, hydrogel, non-woven tissue, felt, and their associations; a scaffold for cell cultures; for use in surgery (e.g. pelvic, abdominal, spinal, cardiac, vascular, ophthalmic, orthopaedic, otorhinolaryngological and plastic-aesthetic surgery), haemodialysis, cardiology, angiology, dermatology, ophthalmology, otorhinolaryngology, dentistry, orthopaedics, gynaecology, urology, in extracorporeal blood circulation and oxygenation, and in cosmetics; as a filler in plastic-aesthetic surgery; as substitutes for the vitreous humor in ophthalmology; useful in the prevention of surgical adhesions of tissues and hypertrophic scars; for the preparation of surgical glues; and as vehicling agent for the preparation of slow release pharmaceutical composition); for coating a biomedical object (e.g. bypass, venous catheter, shunt, catheter, guide channel, probe, cardiac valve, artificial tendon, bone and cardiovascular replacements, contact lens, soft tissue replacement, replacements of animal origin, blood oxygenators, artificial kidney, heart, pancreas and liver, blood bag, syringe, surgical instrument, filtration system, laboratory instrument, containers for cells and tissues cultures and for the regeneration of cells and tissues, support for peptides, proteins and antibodies and in healthcare and surgical articles (e.g. microspheres, nanospheres, membranes, sponges, threads, films, gauzes, guide channels, hydrogels, non-woven tissues, felts, and their associations); in a pharmaceutical preparation and in association with radioactive and non-radioactive substances to be used in contrast systems, for the preparation of markers in vivo diagnostics for the identification and treatment of tumoral or damaged tissues (claimed).

ADVANTAGE - (a) exhibits different chemical-physical properties according to the degree to which they are crosslinked.

Dwg.0/0

TECH UPTX: 20020610

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: Preparation of (a) involves:

(i) controlling the N-deacetylation of **hyaluronic acid** or its derivative to obtain the corresponding partially N-deacetylated

**hyaluronic acid** or its derivative; and
(ii) Ugi's condensation of the partially N-deacetylated **hyaluronic acid** or its derivative with an aldehyde and an isocyanide.
The partial N-deacetylation in the step (i) is carried out by using a hydrazine or hydrazine monohydrate, followed by addition of hydrazine sulfate. Step (i) is carried out at 40-90 degrees C (preferably 40 degrees C) for 8-48 hours. The step (ii) is carried out at room temperature by adding an excess of aldehyde (A') or an isocyanide (B1) to a water solution of the partially N-deacetylated **hyaluronic acid** or its derivative.
Preferred Components: (A') is an optionally substituted 1-20C aldehyde of G series (preferably formaldehyde, acetaldehyde or glyceraldehyde, especially formaldehyde) and is liquid at room temperature. The isocyanide is an optionally substituted isocyanide of G series (preferably cyclohexyl isocyanide or tert-butyl isocyanide).
Preferred Compound: The partially N-deacetylated **hyaluronic acid** or its derivatives has a N-deacetylation of 1-50 (preferably 5-30)%. (a) have a degree of **crosslinking** of 1-50 (preferably 5-30)%. The **hyaluronic acid** derivative is a partial ester of **hyaluronic acid** esterified with alcohol of G; hemiesters of succinic acid or heavy metal salts of the hemiesters with **hyaluronic acid** or with its partial esters; O-sulfated **hyaluronic acid** and its derivative; amide of **hyaluronic acid** or its derivative with an **amine** of G; percarboxylated **hyaluronic acid** and its derivative; **hyaluronic acid** salt with (A); or **hyaluronic acid** salt with heavy metal.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The pharmacologically active substance is antibiotic, anti-infective, antimicrobial, antiviral, antifungal, cytostatic, anticancer, anti-inflammatory, wound healing agent, anaesthetic, cholinergic or adrenergic agonist and antagonist, antithrombotic, anticoagulant, haemostatic, fibrinolytic or thrombolytic. The biologically active substance is protein or its fragment, peptide and polynucleotide, growth factor, enzyme, vaccine and substance used in the treatment of diseases associated with genetic defects, deforming and hereditary diseases.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The heavy metal is a metal selected from the 4th, 5th and 6th period of the periodic table of elements (preferably silver, cobalt, iron, copper, zinc, arsenic, strontium, zirconium, antimony, gold, cesium, tungsten, selenium, platinum, gallium, ruthenium, bismuth, tin, titanium or mercury).

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The natural polymer is collagen or its coprecipitate, glycosaminoglycan, cellulose, polysaccharide in the form of gel, starch or natural gum. The gel is chitin, chitosan, pectin or pectic acid, agar, agarose, xanthan, gellan, alginic acid or the alginate, polymannan or polyglycan. The semisynthetic polymer is the collagen **cross-linked** with an agent (A1). The synthetic polymer is polylactic acid, polyglycolic acid, their copolymers or their derivatives, polydioxane, polyphosphazene, polysulfonic resin, polyurethane or polytetrafluoroethylene (PTFE). (A1) is aldehydes or its precursors, dicarboxylic acid or its halide, diamine, derivative of the cellulose, **hyaluronic acid**, chitin or chitosan, xanthan, pectin or pectic acid, polyglycan, polymannan, agar, agarose, natural gum or glycosaminoglycan. The biomaterial is in association with fibrin, and optionally with other biologically active substance.

L9 ANSWER 8 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-291915 [33] WPIDS
DNN N2002-227914 DNC C2002-085730

TI Capsule useful in in vitro bioassays for e.g. optical detection of target molecules, comprises encapsulated solid particles of signal-generating organic substances and carries affinity molecules on the outer surface.

DC A89 B04 D16 S03

IN CARUSO, F; LEHMANN, M; RENNEBERG, R; TRAU, D

PA (BIOG-N) BIOGNOSTIC AG; (EIGH-N) 8SENS.BIOGNOSTIC AG

CYC 96

PI WO 2002012888 A2 20020214 (200233)* EN 49p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
DE 10042023 A1 20020228 (200233)
AU 2001091746 A 20020218 (200244)

ADT WO 2002012888 A2 WO 2001-EP9114 20010807; DE 10042023 A1 DE 2000-10042023 20000808; AU 2001091746 A AU 2001-91746 20010807

FDT AU 2001091746 A Based on WO 200212888

PRAI DE 2000-10042023 20000808

AB WO 200212888 A UPAB: 20020524
NOVELTY - A capsule that encapsulates solid particles of a signal generating organic substance (a) and that carries on the outer surface affinity molecules for specific recognition of and binding to target molecules, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) optical, electrochemical or chemical detection of at least target molecules in a sample using affinity-based interactions between the target molecule and the affinity molecule, comprising:

(i) incubating the target molecules with the capsules;

(ii) separating the resulting target-affinity molecule complex from the capsules with unreacted affinity molecules on their surface,

(iii) releasing and dissolving the encapsulated solid particles of (a) by treating the complex with physical or chemical method, and

(iv) detecting or qualifying the signal which is generated by the released and dissolved signal-generating substances and which is directly or indirectly related to the amount of the target molecules; and

(2) a kit for optical, electrochemical or chemical detection of target molecules in a sample comprising either the capsules and a dipstick, or the capsules, agents for the modification of affinity molecules to make them suitable to bind to the surface of the capsules, agents for performing the binding reaction between the capsules and the affinity molecules and a dipstick.

USE - The capsule is used in in vitro bioassays for optical, electrochemical or chemical detection of target molecules together with a dip-stick (claimed), particularly in fluorescence immunoassays.

ADVANTAGE - The capsule provides very good sensitivity, a low detection limit and an enhancement of the detection signal related to the amount of the target molecule in the detection method in comparison with the methods known in the prior art, and provides a detection process with a high signal amplification.

Dwg.0/5

TECH UPTX: 20020524
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: The release of the signal-generating substances is achieved by chemical methods (preferably by treatment with an organic solvent or with an enzyme, ribozyme or aptamer or by changing the pH or ionic strength value), or by a physical method (preferably ultrasonic disintegration, electric impulse or osmotic shock).
Preferred Capsule: The affinity molecules are conjugated or bound directly or via linker molecules to the outer surface of the capsule. The encapsulated solid particles of (a) are crystals, amorphous or lyophilized

particles, spray dried particles and/or milled particles, and have a particle size of 10 nm - 10 micrometers (preferably smaller than 1 micrometer). The capsule walls consist of one or multiple polyelectrolyte layers or layers of substances bearing functional groups and being adsorbed or covalently linked. The polyelectrolytes in one layer and/or between the layers are **cross-linked**.
TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The affinity molecule is a peptide or protein, nucleic acid, carbohydrate, ligand with low molecular weight and/or molecular imprinted polymer. The peptide or protein is an antibody, receptor, antigen, lectin, avidin, oligopeptide, lipoprotein, glycoprotein, peptide hormone, allergene or its respective part. The nucleic acid is a single or double stranded DNA, RNA, oligonucleotide, ribozyme, aptamer or its part. The low molecular weight ligand is biotin or its derivative, steroid or hormone, a cofactor or coenzyme, activator, inhibitor, pseudosubstrate or prosthetic group of an enzyme, a drug, a pesticide, an allergen or digoxine or a hapten. The linker molecule is a biomolecule (preferably avidine, streptavidine, neutravidine, protein A, protein G, lectine or a low molecular weight **crosslinker**). The encapsulated solid particles of (a) are low molecular substances selected from fluorophore, luminophore, chromophore, enzyme substrates, prosthetic group or redox active substances selected from redox mediators or electrodeactive substances) or high-molecular substances selected from enzymes or their precursors, bioluminogenic or fluorogenic proteins, nucleic acids, ribozymes or aptamers).

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The carbohydrates are mono-, oligo- or poly-saccharides, glycolipids, or proteo-polysaccharides or their respective parts. The polyelectrolytes or substances bearing functional groups are organic polymers (preferably a polymer selected from **polyamine**, polysulfonic acid, polyglycolic acid, polyactic acid, polyamide, poly-2-hydroxy butyrate, polycaprolactone, fluorescent labelled polymer and/or its copolymers) and/or biopolymer (preferably polyamino acid, especially peptide or polylysine), polycarbohydrate (preferably dextrin, pectin, alginate, glycogen, amylose, chitin, chondroitin or **hyaluronic acid**), polyoligonucleotide (preferably DNA, RNA or oligonucleotide) or modified biopolymer (preferably carboxymethyl cellulose, carboxymethyl dextran or lignin sulfonate)).

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Capsule: The substances with functional groups are substances bearing -COOR, -NRR1, -SR, -OR, -SSR, -C(O)R, -OC(OH)RR1 or -SC(O)R groups.
R and R1 = H or linear or branched alkyl.
The organic solvent is an alcohol (preferably ethanol or methanol), ketone (preferably acetone), ester (preferably ethyl ester), aromatic (preferably toluene), sulfoxide (preferably dimethylsulphoxide (DMSO)), ether (preferably dimethylether), chloroform or their mixtures with one another and with water.

L9 ANSWER 9 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-034328 [04] WPIDS
DNC C2002-009564
TI Producing 3-dimensional objects under mild conditions, using 3-dimensionally movable dispenser to supply material into medium, useful for producing biomedical objects such as implants.
DC A32 A96 B04 D16 D22 P42
IN JOHN, H; LANDERS, R; MUELHAUPT, R
PA (ENVI-N) ENVISION TECHNOLOGIES GMBH
CYC 31
PI WO 2001078968 A1 20011025 (200204)* DE 40p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU BR CA CN CZ IL JP KR MX SG US ZA
DE 10018987 A1 20011031 (200204)
AU 2001020036 A 20011030 (200219)

ADT WO 2001078968 A1 WO 2000-EP12102 20001201; DE 10018987 A1 DE 2000-10018987 20000417; AU 2001020036 A AU 2001-20036 20001201
FDT AU 2001020036 A Based on WO 200178968
PRAI DE 2000-10018987 20000417
AB WO 200178968 A UPAB: 20020117
NOVELTY - Preparing a 3-dimensional object, comprising placing an outlet opening of a 3-dimensionally moveable dispenser in a non-gaseous medium (A) in a container, supplying a material (B) via the dispenser into (A), so that (A) hardens on addition of (B) or (B) forms solid structures on contact with (A), and moving the dispenser into appropriate positions to form a solid 3-dimensional structure, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for apparatus for the process, comprising a container for (A), and the 3-dimensionally moveable dispenser for (B), having an outlet which can be positioned below the filling level for (A) in the container.

USE - The process and apparatus are specifically used for producing biomedical or biologically active objects containing biologically or pharmaceutically active agents, especially additives or matrix materials selected from proteins, growth factors, living cells, **hyaluronic acid**, gelatin, collagen, alginic acid (or its salt) or chitosan (or its salt) (claimed). The objects include implants for prolonged drug release (e.g. for direct post-operative introduction into the brain of brain tumor patients), supported cells for culture in vitro or bone cements.

ADVANTAGE - The 3-dimensional structures of controlled shape (e.g. microdots, microstrings or tubes) are produced without irradiation or use of high temperatures, and can contain heat-sensitive additives such as human cells.

DESCRIPTION OF DRAWING(S) - The drawing shows a schematic diagram of an apparatus for producing biomedical objects.

Container 1
Medium 2
Material components 3
Dispenser 4
Outlet 5
Controller 6
Material receiving platform 8
Axes of motion of the dispenser x, y, z.
Dwg.1/4

TECH UPTX: 20020117
TECHNOLOGY FOCUS - POLYMERS - Preferred Process: The objects are formed by precipitation or co-reaction (specifically interfacial polymerization, polycondensation or polyelectrolyte complex formation). In particular (A) is water, gelatin and/or aqueous **polyamine** solution, and (B) consists of liquid, molten or reactive oligomers or polymers, monomers, gels, pastes, plastisols, solutions, co-reactive 2-component systems and/or dispersions. (B) especially consists of a gel of single- or multi-component silicone rubber, a paste of oligomers or polymers containing (in)organic fillers, an isocyanate/polyamide co-reactive system, or polyurethanes.

L9 ANSWER 10 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-010509 [01] WPIDS
DNN N2002-008807 DNC C2002-002501
TI Biocompatible material useful in sealing vascular punctures, preventing post-operative adhesions, repairing tissue voids, embolizing arterio-venous malformation, or filling an aneurysm, comprises a mixture of protein and a polymer solution.
DC A96 B04 B07 D16 D22 P31
IN CRUISE, G M; HNOJEWYJ, O; MILO, C
PA (NEOM-N) NEO MEND INC
CYC 93
PI WO 2001066017 A1 20010913 (200201)* EN 63p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001038635 A 20010917 (200204)

ADT WO 2001066017 A1 WO 2001-US5694 20010222; AU 2001038635 A AU 2001-38635 20010222

FDT AU 2001038635 A Based on WO 200166017

PRAI US 2000-520856 20000307

AB WO 200166017 A UPAB: 20020105

NOVELTY - A biocompatible material comprises a mixture of a protein solution (A) and a polymer solution (B). (B) includes a derivative of a hydrophilic polymer with a functionality of at least 3. On mixing, (A) and (B) cross-link to form a non-liquid, three-dimensional network.

DETAILED DESCRIPTION - A biocompatible material comprises a mixture of a protein solution (A) and a polymer solution (B). (B) includes a derivative of a hydrophilic polymer with a functionality of at least 3. On mixing, (A) and (B) cross-link to form a non-liquid, three-dimensional network. The network degrades to a liquid form. The polymer includes a degradation control region to achieve a desired degradation period and/or a cross-linking group to achieve a desired cross-linking period.

An INDEPENDENT CLAIM is also included for a system (S1) comprising (A), (B) and instructions for forming a mixture of (A) and (B), and applying the mixture to seal a vascular puncture site, seal tissue from liquid leaks (preferably blood), seal solid or gas leaks, prevent post-operative adhesions, to repair a tissue void, augment tissue, to embolize an arterio-venous malformation, or to fill an aneurysm.

ACTIVITY - Vulnerary.

No supporting data given.

MECHANISM OF ACTION - None given in the source material.

USE - For use in systems to seal a vascular puncture site (degradation period (DP) of approximately 30 days, and cross-linking period (CP) of 15 - 60 seconds); seal tissue from liquid leaks (preferably blood) or solid leaks (DP of approximately 30 days and CP of less than 1 second); to repair a tissue void (DP of 30 - 60 days, and CP of 5 seconds); to prevent post-operative adhesions (DP of 5 - 30 days, and CP of less than 1 second); to augment tissues (DP of approximately 1 year, and CP of approximately 120 seconds); to embolize an arterio-venous malformation (CP of 30 - 120 seconds); to fill an aneurysm or deliver a pharmaceutical (DP of approximately 1 year, and CP of 5 - 30 seconds); and to deliver cells (DP of approximately 1 week - 6 months, and CP of 5 - 30 seconds) (all claimed).

ADVANTAGE - The materials are cost effective. The material flows into the surface irregularities before solidification and enhances patient safety. Unlike the prior art, no emboli is formed if the biomaterial enters the bloodstream before solidification. The hydrogel formed from the material possesses a high adhesive and cohesive strength.

Dwg.0/6

TECH UPTX: 20020105

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The degradation control region comprises at least one hydrolytically or enzymatically degradable moiety. The hydrolytically degradable moiety is selected from saturated or unsaturated di-acid, poly(glycolic acid), poly(DL-lactic acid), poly(L-lactic acid), poly(xi-caprolactone), poly(delta-valerolactone), poly(gamma-butyrolactone), poly(amino acid), poly(anhydride), poly(orthoester), poly(orthocarbonate) or poly(phosphoester). The polymer is of formula PEG-(DCR-CG)n (having a multi-armed polymer structure). (B) includes derivative of a polymer selected from poly(ethylene glycol) (PEG), poly(ethylene oxide), poly(vinyl alcohol), poly(vinylpyrrolidone), poly(ethyloxazoline), poly(ethylene glycol)-co-poly(propylene glycol) block copolymers,

electrophilically derivatized polysaccharides, carbohydrates, or proteins (preferably PEG). The PEG has a molecular weight from 1,000 - 30,000 (especially 10,000 - 15, 000) g/mole.
PEG = poly(ethylene glycol);
DCR = degradation control region;
CG = **cross-linking** group;
n = at least 3.
Preferred Conditions: The degradation period (DP) is from 1 - more than 500 (preferably 5 - 30) days. The **cross-linking** period (CP) is from less than 1 second - greater than 10 hours (preferably less than 1 second - 10 minutes, especially less than 1 second - 2 minutes).

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The **cross-linking** group reacts with at least one thiol, **amine** or aldehyde. The **cross-linking** group is selected from active ester, epoxide, oxycarbonylimidazole, nitrophenyl carbonate, tresylate, mesylate, tosylate, isocyanate, vinyl sulfone, N-ethyl maleimide, iodoacetamide or orthopyridyl disulfide (preferably an ester of N-hydroxysuccinimide). (A) includes a buffer (preferably carbonate or phosphate). The material additionally comprises a color changing agent. The agent changes its color when **cross-linking** of the mixture takes place. The agent undergoes color change in response to the change in pH. The agent exhibits a first color when the mixture is in a liquid state (preferably when the mixture is in transition between a liquid and the non-liquid state) and a second color, when the mixture form the non-liquid, three-dimensional network. The agent is xylenol blue, phenol red, (a mixture of these), phenolphthalein, ortho-cresolphthalein and/or bromothymol blue.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Materials: The enzymatically degradable moiety is Leu-Glyc-Pro-Ala (collagenes sensitive linkage) or Gly-Pro-Lys (plasmin sensitive linkage). (A) comprises at least one non-immunogenic, hydrophilic protein, water soluble derivative of hydrophobic protein, recombinant or natural human serum albumin (at most 25%). The non-immunogenic, hydrophilic protein is selected from serum, serum fractions, solution of albumin, gelatin, antibodies, fibrinogen, or serum protein. The water soluble derivative of a hydrophobic protein is selected from solution of collagen, elastin, chitosan, or **hyaluronic acid**. (A) and (B) comprise at least one hybrid protein or synthetic amino acid sequence.

L9 ANSWER 11 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-648293 [74] WPIDS
DNC C2001-191243
TI Clathrate complex useful in the treatment of disorders in the field of rheumatology such as arthritis, osteoarthritis is formed by association of high molecular weight hyaluronic acid derivatives.
DC A11 A96 B04
IN BYSTRICKY, S; KOGAN, G; MACHOVA, E; MENDICHI, R; SOLTES, L; STEINER, B
PA (FIDI-N) FIDIA FARM SPA; (SLSC-N) SLOVAK ACAD SCI INST EXPERIMENTAL PHARMA
CYC 95
PI WO 2001066601 A1 20010913 (200174)* EN 23p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001052180 A 20010917 (200204)
ADT WO 2001066601 A1 WO 2001-EP2722 20010312; AU 2001052180 A AU 2001-52180 20010312
FDT AU 2001052180 A Based on WO 200166601
PRAI SK 2000-358 20000310

AB WO 200166601 A UPAB: 20011217
NOVELTY - A Clathrate complex is formed by association of a hyaluronic acid derivative (a), a hyaluronic acid derivative (b1), different from (a) and able to form a clathrate with (a) and/or a compound (b2) not having a hyaluronic acid group, but able to form a clathrate with (a).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a medicament containing the clathrate complex as the active ingredient;

(2) a hyaluronic acid derivative with cyclodextrin obtained using a spacer;

(3) preparation of the hyaluronic acid derivative with cyclodextrin involves two steps:

(a) formation of an initial hydrazide group (-CO-NH-NH-CO-) between adipic acid dihydrazide (NH2-NHCO(CH2)4CONH-NH2), as a spacer and carboxylic groups of pre-activated hyaluronic acid; and

(b) a reaction between the second hydrazide function (NH2-NHCO-) of the adipic acid dihydrazide derivative of hyaluronic acid obtained from step (a) with a pre-activated cyclodextrin;

(4) a hyaluronic acid derivative with amantadine;

(5) preparation of the hyaluronic acid derivative with amantadine involving formation of amidic bond between pre-activated hyaluronic acid and amantadine in an aqueous solution in the presence of a buffer;

(6) a pharmaceutical composition containing the hyaluronic acid derivative with cyclodextrin or the hyaluronic acid derivative with amantadine, as the active ingredient in combination with excipients and/or diluents;

(7) a pharmaceutical composition containing the hyaluronic acid derivative with cyclodextrin, obtained by the direct esterification of hyaluronic acid with cyclodextrin, as the active ingredient in combination with excipients and/or diluents;

(8) a medicament comprising obtained by the association of two pharmaceutical compositions in the form of injectable solutions containing the hyaluronic acid derivative with cyclodextrin and the hyaluronic acid derivative with amantadine respectively, as the active ingredients, to obtain an in situ formation of the clathrate;

(9) a controlled release pharmaceutical composition containing the hyaluronic acid derivative with cyclodextrin as the vehicling agent; and

(10) a contrast media containing a radioactive substance in association with the hyaluronic acid derivative with cyclodextrin.

ACTIVITY - Osteophathic; Antiarthritic; Antirheumatic; Dermatological; Gynaecological; Ophthalmological; Gynecological; anti-inflammatory; Cytostatic; Cerebroprotective; Neuroprotective; Antianginal; Vulnerary.

MECHANISM OF ACTION - None given.

USE - In the treatment of disorders in the fields such as dermatology, ophthalmology (e.g. eye infection and inflammation such as conjunctivitis), gynecology, oncology, angiology, neurology, orthopaedics or rheumatology (all claimed), in need of restoration of viscoelasticity e.g. conjunctivitis, rheumatoid arthritis, osteoarthritis, malignant tumors and skin wounds.

ADVANTAGE - The clathrate complexes formed with the high molecular weight hyaluronic acid derivatives do not exhibit a very high viscosity in addition to possessing biocompatibility, (bio) degradibility, complete resorption, non-immunogenicity, very low and rare pyrogenicity, and increased penetrability and permeability, compared to the prior art clathrate complexes

Dwg.0/3

TECH UPTX: 20011217
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Clathrate: The clathrate is selected from clathrate (C1) containing the **hyaluronic acid** derivative with cyclodextrin (I) as (a) and the **hyaluronic acid** derivative with amantadine (II) as (b1),

clathrate (C2) containing (I) as (a) and a water-soluble natural, semisynthetic or synthetic polymer as (b2); or clathrate (C3) containing (I) as (a) and a polymerized cyclodextrin as (b2) (preferably C1). (C1) has a molecular weight between 500 - 25,000 (preferably 2,000 - 20,000) kDa and a ratio of (I):(II) between 10:90 - 90:10 (preferably 80:20 - 50:50).
Preferred Components: The cyclodextrin is selected from alpha-, beta- or gamma-cyclodextrin, propyl-beta-cyclodextrin, sulfobutyl-beta-cyclodextrin, or amino or hydrazine-beta-cyclodextrin. The **hyaluronic acid** derivatives have a degree of substitution of the carboxylic function between 0.5 - 50 (preferably 2 - 50)%. (II) has the degree of substitution between 0.5 - 25 (preferably 2 - 10)%. The starting reactant **hyaluronic acid** has a molecular weight between 100 - 2,000 kDa.
Preferred Method: The step (a) is carried out in the presence of an aqueous buffer solution at pH 5.5 containing sodium 2(N-morpholino)-ethanesulfonate, and adipic acid dihydrazide is added to **hyaluronic acid** activated with 1-ethyl-3-(3-dimethyl-aminopropyl)-carbodiimide (c). The step (b) is carried out by adding the **hyaluronic acid** derivative with adipic acid di-hydrazide from step (a) to a water solution of cyclodextrin previously activated with 1-cyano-4-dimethyl-aminopyridinium tetrafluoro-borate in acetonitrile in the presence of triethyl-**amine** and the reaction is stopped by adding ethanolamine. The amantadine activator is 1-ethyl-3-(3-dimethyl-aminopropyl)-carbodiimide and the buffer is 2(N-morpholino)-ethanesulfonate.

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: In (C2), (b2) as the natural polymers are selected from collagen or its coprecipitates with glycosaminoglycans, cellulose, polysaccharides, agarose, xanthane, gellan, alginic acid or its salts or esters, polymannan, polyglycans, starch or natural gums, (b2) as the semisynthetic polymers are selected from collagen **cross-linked** with **crosslinking** agents, derivatives of cellulose, **hyaluronic acid**, chitin, chitosan, gellan, xanthane, pectin or pectic acid, polyglycans, polymannan, agar, agarose, natural gum or glycosaminoglycans, and (b2) as the synthetic polymers are selected from poloxamers (preferably polyethyleneglycol having molecular weight of 2,000 Da). In (C3) the polymerized cyclodextrin is polymerized beta-cyclodextrin having molecular weight of 91,200 Da.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Medicament: The medicament further contains a low molecular weight active ingredient; and a biologically active substance and/or a cellular material, in alternative to or in addition to the active ingredient. In the medicament obtained by the association of the pharmaceutical compositions containing (I) and (II) respectively, the active ingredient, the biologically active substance and/or the cellular material; are coupled to cyclodextrin. The controlled release pharmaceutical composition contains the active ingredient or the biologically active substance. Preferred Components: The active ingredient is selected from non-steroidal or steroidal anti-inflammatory drug, antibiotic or antitumoral (preferably proxicam). The biologically active substance is selected from growth factors or cytokines. The cellular material is selected from osteocytes, chondrocytes, stem cells or mesenchymal cells.

L9 ANSWER 12 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-559070 [63] WPIDS
DNC C2001-166372
TI Encapsulation of an uncharged solid particle material to prepare capsule useful in pharmacy, involves treating the material with an amphiphilic substance and coating the material with a layers of a charged polyelectrolyte.

DC A96 A97 B07 C07 D13 D16 G05
IN CARUSO, F; MOEHWALD, H; RENNEBERG, R; TRAU, D
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN
CYC 28
PI EP 1116516 A1 20010718 (200163)* EN 23p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
DE 10001172 A1 20010726 (200163)
WO 2001051196 A1 20010719 (200163) EN
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: JP US
ADT EP 1116516 A1 EP 2000-111523 20000529; DE 10001172 A1 DE 2000-10001172 20000113; WO 2001051196 A1 WO 2001-EP329 20010112
PRAI DE 2000-10001172 20000113
AB EP 1116516 A UPAB: 20011031
NOVELTY - Encapsulation of an uncharged solid particle material, comprising treating the solid particle material with an amphiphilic substance, and subsequently coating the material with a layer of a charged polyelectrolyte or with a multilayer comprising alternating layers of oppositely charged polyelectrolytes, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing capsules having a polyelectrolyte shell, comprising performing the novel method, and removing the core of the uncharged solid particles;

(2) a polyelectrolyte capsule, obtained by the novel method, or the method of (1); and

(3) a composition containing capsules in a dried form and having a monodisperse size distribution.

USE - For encapsulation of an uncharged solid particle material and for preparation of a capsule for the encapsulation of drugs and as reaction chambers. The capsule is useful in sensoric, surface-analytic or information technology applications and in pharmacy, medicine, food technology, biotechnology, cosmetics or in printing applications and as slow, targeted or controlled release systems. (All claimed).

ADVANTAGE - The drugs are released with a constant release rate and in small amounts over a long time period. The capsule thickness and permeability for the controlled release of the encapsulated material can be controlled in a predetermined manner.

Dwg.0/6

TECH UPTX: 20011031
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The solid material has a low solubility in water or is water insoluble. The solid material is an organic material, a bio-material or an inorganic material. The solid material is selected from drugs, vitamins, nutrients, hormones, growth factors, pesticides, antibiotics and/or preservatives. The solid material is selected from single crystals, amorphous or lyophilized materials, spray dried materials and/or milled materials. The solid material is a synthetic material or a material isolated from natural sources or a chemical modified isolated material. The amphiphilic substance is selected from ionic surfactant, preferably a cationic and/or an anionic surfactant, phospholipid or amphiphilic polyelectrolyte. The cationic surfactant is selected from quarternary ammonium salts, preferably didodecyldimethylammonium bromide, alkyltrimethylammoniumbromide, preferably dodecyltrimethylammonium bromide or palmithyltrimethylamonium bromide, and/or N-alkyl pyridinium salts, tertiary **amine**, preferably cholesteryl-3beta-N-(dimethyl-aminoethyl) carbamate, or secondary or primary **amine**. The anionic surfactant is selected from alkylsulfonate, preferably dodecylsulfate, laurylsulfate or olefinsulfonate, preferably sodium n-dodecylbenzenesulfonate, and/or alkylsulfates or fatty acids, preferably dodecanoic acid sodium salt or phosphoric acids or cholic acids or fluoro organics, especially lithium 3-(2-(perfluoroalkyl)ethylthio)propionate.

Preferred Process: The capsule thickness and permeability for the controlled release of the encapsulated material is controlled by the nature of the surfactant, the number of layers, the nature of the polyelectrolyte, the nature of the nanoparticle or biomolecule and an additional **cross-linking** step. The hollow capsules are produced from the encapsulated material by removal of the core material by exposure to an organic solvent in which the material is soluble or an acid and/or alkaline solvent in which the material is forming a soluble salt. The hollow capsules are re-dispersed in an aqueous solvent and/or an organic solvent. A drug is incorporated into the capsules. The size of pores within the capsule wall is controlled by the kind of amphiphilic substance used and/or the coating conditions of the amphiphilic substance. The capsule comprises no detectable residue of the solid core material and has a final shape, which is determined by the uncharged solid core material.

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The amphiphilic substance is a polymeric substance which provides charged groups and hydrophobic sides, preferably poly(styrenesulfonate), or is a block-copolymer, preferably poly(ethylethylene-blockstyrene sulfonic acid). The polyelectrolyte is selected from organic polymer, biopolymer and/or inorganic polymer or a block copolymer. The polyelectrolyte is a linear and/or a non-linear polymer. The organic polymer is selected from biodegradable polymers, preferably polyglycolic acid, polylactic acid, polyamides, poly-2-hydroxy butyrate, polycaprolactone, poly (lactic-co-glycolic) acid, fluorescent labelled polymer, conducting polymer, liquid crystal polymer, photo conducting polymer, photochromic polymer and/or their copolymers. The biopolymer is selected from polyamino acid, preferably peptide, S-layer protein, poly carbohydrate, preferably dextrin, pectin, alginate, glycogen, amylose, chitin, chondroitin, **hyaluronic acid**, poly nucleotide, preferably DNA or RNA, oligonucleotide and/or modified biopolymer, preferably carboxymethyl cellulose, carboxymethyl dextran or lignin sulfonate. The inorganic polymer is selected from polysilane, polysilanole, polyphosphazene, polysulfazene, polysulfide and/or polyphosphates.
Preferred Process: The polyelectrolyte is **cross-linked** after templating. The **cross-linking** is provided between the polymers in one layer and/or between the layers. The charged nanoparticles or biomolecules are deposited as capsule materials. The excessive material of amphiphilic substance, polyelectrolytes and/or nanoparticles and biomolecules, that are not contributed to form the coating, are separated after each coating step. The encapsulated material is forming a stable suspension in an aquatic phase.

L9 ANSWER 13 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-420122 [45] WPIDS
DNC C2001-127218
TI **Crosslinked** copolymers, biodegradable in the digestive tract, suitable for the controlled release of pharmaceuticals.
DC A11 A14 A96 B07
IN DIANCOURT, F; DUCOS, C; LABARRE, D; LAMBERT, N
PA (SCRC) SCRAS SOC CONSEILS RECH & APPL SCI; (SCRC) SAS SOC CONSEILS RECH & APPL SCI; (SCRC) SOC CONSEILS RECH & APPL SCI
CYC 94
PI FR 2799196 A1 20010406 (200145)* 17p
AU 2000076706 A 20010510 (200145)
WO 2001025295 A1 20010412 (200145) FR
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

NO 2002001573 A 20020531 (200248)
ADT FR 2799196 A1 FR 1999-12363 19991004; AU 2000076706 A AU 2000-76706 20001003; WO 2001025295 A1 WO 2000-FR2731 20001003; NO 2002001573 A WO 2000-FR2731 20001003, NO 2002-1573 20020403
FDT AU 2000076706 A Based on WO 200125295
PRAI FR 1999-12363 19991004
AB FR 2799196 A UPAB: 20010813
NOVELTY - **Crosslinked** copolymers from an uncrosslinked polycarboxylic acid copolymer and a **crosslinking** agent having at least two amino groups. The polycarboxylic acid copolymer has a polysaccharide chain attached through a covalent bond to least one other non-**crosslinked** and non-saccharidic polymer, at least one of these polysaccharidic or non-saccharidic copolymers is polycarboxylic.
USE - The polymers are biodegradable by the microbial flora of the colon and are useful as controlled release carriers for pharmaceuticals (claimed). The copolymers have pharmaceutical, cosmetic, biomedical, veterinary, chemical, agrochemical and agro-alimentary applications. In particular they are carriers for pharmaceuticals to be liberated in the colon or in the upper digestive tract, such as steroids, anti-inflammatories (steroidal and non-steroidal), antineoplastics, antispasmodics, and chemotherapeutic agents.
Dwg.0/0
TECH UPTX: 20010813
TECHNOLOGY FOCUS - POLYMERS - Preferred Polymers: Suitable non-carboxylic polysaccharide copolymers include agarose, agaropectin, amylose, amylopectin, arabino-galactane, carrageenans, cellulose, methyl cellulose, chitosan, dextran, fucans, fucoidans, tragacanth, arabic, caruba and guar gums, or pullan. Suitable polycarboxylic polysaccharides include **hyaluronic acid**, chondroitin sulfate, heparin, dermatan sulfate, heparan sulfate, keratan sulfate, glycosaminoglycans, pectinic acid and alginic acid. Suitable non-saccharidic non-carboxylic polymers include poly(vinyl acetate), poly(vinyl alcohol), poly(acrylic esters), poly(methacrylic esters), poly(methylacrylamides), and **poly** (acrylamides). Suitable **amines** may be natural or synthetic, and are preferably diamines, these include ethylene diamine, butane diamine, hexane diamine, heptane diamine, octane diamine, and dodecane diamine

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The products are prepared by mixing the polycarboxylic copolymers with the **crosslinking** agent in an aqueous medium in the presence of an activator such as a carbodiimide, a quinoline, or a mixed anhydride. The non-saccharidic monomer is grafted on to the polysaccharide in an aqueous medium in the presence of a catalyst such as ceric ions.

L9 ANSWER 14 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-354609 [37] WPIDS
DNN N2001-257675 DNC C2001-109770
TI Biocompatible polymeric material, useful for making surgical implants, comprises hyaluronic acid, crosslinked amino-functional polymer gel and water.
DC A14 A25 A96 D22 P34
IN KOZLOVA, T V; SKOBELEVA, V B; ZEZIN, A B
PA (KOZL-I) KOZLOVA T V; (SKOB-I) SKOBELEVA V B; (ZEZI-I) ZEZIN A B
CYC 84
PI WO 2001015749 A1 20010308 (200137)* RU 22p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 2001028082 A 20010326 (200137)
RU 2162343 C2 20010127 (200137)

ADT WO 2001015749 A1 WO 2000-RU352 20000831; AU 2001028082 A AU 2001-28082 20000831; RU 2162343 C2 RU 1999-118961 19990901
FDT AU 2001028082 A Based on WO 200115749
PRAI RU 1999-118961 19990901
AB WO 200115749 A UPAB: 20010704
NOVELTY - Biocompatible polymeric material comprises hyaluronic acid, a crosslinked amino-functional polymer gel and water.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the production of a biocompatible polymeric material by depositing hyaluronic acid on a polymeric support by mixing the components in an aqueous solution at 10 - 80 deg. C and pH 3 - 10 for 2 - 48 hours, and then washing the product with physiological saline.

USE - The material is useful for making surgical implants e.g. for ophthalmic surgery.

ADVANTAGE - The material has good biocompatibility, is highly hydrophilic, has adequate mechanical strength and elasticity, exhibits low protein adsorption, is resistant to proteolytic enzymes, is transparent with a high refractive index, and is capable of forming stable viscoelastic coatings that are retained for long periods on the surface of materials in contact with living tissues.

Dwg.0/0
TECH UPTX: 20010704
TECHNOLOGY FOCUS - POLYMERS - Preferred Polymer Gel: The amino functional polymer is an N,N-dimethylaminoethyl methacrylate polymer, optionally quaternized with methyl chloride or ethyl bromide, or a copolymer prepared by copolymerizing an unsaturated **amine** with a water-soluble ethylenically unsaturated nonionic monomer (especially acrylamide, 2-hydroxyethyl methacrylate or N-vinylpyrrolidone) in an aqueous medium in the presence of a **crosslinking** agent containing at least two double bonds, e.g. N,N'-methylenebisacrylamide or a (poly)ethylene glycol di(meth)acrylate containing 1-13 ethylene glycol units. The gel can be modified with collagen during its preparation or before adding the **hyaluronic acid**.

L9 ANSWER 15 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-201506 [20] WPIDS
DNC C2001-059788
TI Affinity chromatographic matrix with non-covalent bonding between the charged chromatographic matrix and charged polymeric ligand is used to purify biomacromolecules e.g. chondroitinase.
DC B04 D16
IN KHANDKE, K M
PA (AMCY) AMERICAN CYANAMID CO
CYC 1
PI US 6150151 A 20001121 (200120)* 5p
ADT US 6150151 A Cont of US 1993-31158 19930312, US 1994-292162 19940817
PRAI US 1993-31158 19930312; US 1994-292162 19940817
AB US 6150151 A UPAB: 20010410
NOVELTY - Affinity chromatographic matrix comprises a charged polymeric ligand non-covalently bound to an oppositely charged chromatographic matrix, where the charged polymeric ligand is directly bound by an ionic bond to the oppositely charged group on the chromatographic matrix and the ligand is capable of non-covalently binding a biomacromolecule to purify the biomacromolecule.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a process for purification of chondroitinase from crude material with an affinity chromatographic matrix comprised of an anion exchange resin to which chondroitin sulfate is directly bound by a ionic bond, allowing chondroitinase to bind non-covalently to the chondroitin sulfate and washing contaminating proteins through the matrix before dissociation of chondroitinase from the matrix.

USE - The affinity chromatographic matrix is used for purifying a biomacromolecule, in particular for purifying chondroitinase from crude

material using chondroitin sulfate as the ligand (claimed).
ADVANTAGE - As the ligand is non-covalently bound to the matrix by an ionic bond the ligand can be easily washed off the matrix and replaced for subsequent purifications without needing to replace the matrix. The support matrix affinity gel is simple to prepare and has reduced costs compared with covalently coupled gels.
Dwg.0/1

TECH UPTX: 20010410
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Ligand: The ligand is a glycoaminoglycan or a polysaccharide e.g. chondroitin sulfate, deacetylated chondroitin sulfate, heparin sulfate, dermatan sulfate or **hyaluronic acid**.
Preferred Matrix: The charged chromatographic matrix is a gel with positively charged quaternary **amine** or diethylaminoethyl (DEAE) groups. The matrix is ionically charged.
The matrix material is **crosslinked** agarose, **crosslinked** dextran, **crosslinked** cellulose, **crosslinked** dextran and bisacrylamide or is based on plastic or silica polymers. The anion exchange resin is Q-Sepharose.
Preferred Process: The chondroitinase is loaded on to the affinity chromatographic matrix at pH 7-8.

L9 ANSWER 16 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-168234 [17] WPIDS
DNN N2001-121365 DNC C2001-050121
TI Reducing adsorption on charged surfaces or substrates, e.g. of analytical device, sensor or implant, by applying polyionic multifunctional copolymer having side-chains grafted onto charged polyionic backbone.
DC A89 B04 D22 J04 P34 S03
IN ELBERT, D L; FINKEN, S; HOFER, R; HUBBELL, J A; RUIZ-TAYLOR, L; SPENCER, N D; TEXTOR, M
PA (EIDG-N) EIDGENOESSISCHE TECH HOCHSCHULE ZUERICH; (HUBB-I) HUBBELL J A; (ELBE-I) ELBERT D L; (FINK-I) FINKEN S; (HOFE-I) HOFER R; (RUIZ-I) RUIZ-TAYLOR L; (SPEN-I) SPENCER N D; (TEXT-I) TEXTOR M
CYC 91
PI WO 2000065352 A1 20001102 (200117)* EN 92p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000046846 A 20001110 (200117)
EP 1190252 A1 20020327 (200229) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002128234 A1 20020912 (200262)
ADT WO 2000065352 A1 WO 2000-US11708 20000428; AU 2000046846 A AU 2000-46846 20000428; EP 1190252 A1 EP 2000-928641 20000428, WO 2000-US11708 20000428; US 2002128234 A1 Provisional US 1999-131391P 19990428, Provisional US 1999-131402P 19990428, Provisional US 2000-184616P 20000224, US 2000-560472 20000428
FDT AU 2000046846 A Based on WO 200065352; EP 1190252 A1 Based on WO 200065352
PRAI US 2000-184616P 20000224; US 1999-131391P 19990428; US 1999-131402P 19990428; US 2000-560472 20000428
AB WO 200065352 A UPAB: 20010328
NOVELTY - A method for reducing adsorption on charged surfaces or substrates (A) involves treating (A) with a polyionic multifunctional copolymer (I) comprising non-interactive polymer side-chains grafted onto a charged polyionic backbone, where (A) and (I) have opposite charges.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the (I)-coated (A) produced by the method.
USE - The use of the coated product is claimed: (i) for

quantitatively or qualitatively determining or detecting an analyte, specifically a polynucleotide, peptide, protein, carbohydrate, sugar or glycoprotein, particularly where the amount of analyte immobilized on the coated surface is determined by measuring electromagnetic radiation (e.g. utilizing absorption, scattering, emission or thermal phenomena); or (ii) to modify cell to surface interactions, especially where the substrate is a material for use in cell culture, purification of materials from cells, performing assays or implantation in a patient (especially as a stent, catheter, prosthesis, implant or graft). Typical applications of coated sensors are in diagnostic assays (often involving complex sample mixtures such as blood) and in screening assays for DNA/RNA or protein libraries.

ADVANTAGE - In analytical devices or sensors the (I) coating promotes specific recognition of the target analyte while minimizing non-specific adsorption of other molecules in the sample solution. The coatings can incorporate chemical, biochemical or biological groups to provide specific recognition, interaction and binding properties for target molecules. Mixtures of differently functionalized (I), or of functionalized and non-functionalized (I), can be used to allow detection of multiple analytes. The coatings are stable, and can be applied simply, rapidly and inexpensively.

Dwg.0/12

TECH UPTX: 20010328

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymers: The backbone has a cationic charge at pH greater than 4, and is selected from polymers of appropriate aminoacids, polysaccharides, **polyamines**, polymers of quaternary amines and charged synthetic polymers. In particular the cationic backbone comprises one or more units selected from lysine, histidine, arginine or ornithine (all D-, L- or DL), aminated neutral polysaccharide derivatives, optionally partially deacetylated chitosan, poly-(aminostyrene), poly-(amino(meth)acrylate) (including the N-methyl, N-ethyl, N,N-dimethyl or N,N-diethyl derivative), polyethyleneimine, poly-(N,N,N-trimethylaminoacrylate chloride), poly-(methacrylamidopropyl-trimethylammonium chloride), polyaminoethylene, poly-(aminoethyl)-ethylene, polyaminoethylstyrene and N-alkyl derivatives.

Alternatively the backbone has an anionic charge at pH greater than 4, and is selected from polymers of appropriate aminoacids, polysaccharides and charged synthetic polymers with pendant negatively charged groups. In particular the anionic backbone comprises one or more units selected from polyaspartic acid, polyglutamic acid, alginate, carrageenan, furcellaran, pectin, xanthan, **hyaluronic acid**, heparin, heparan sulfate, chondroitin sulfate, dermatan sulfate, dextran sulfate, poly(meth)acrylic acid, oxidized cellulose, carboxymethyl cellulose, croscarmelose, maleic acid polymers and fumaric acid polymers.

The non-interactive polymer is selected from polyalkylene glycols, polyalkylene oxides, neutral water-soluble polysaccharides, polyvinyl alcohol, polyvinyl pyrrolidone, phosphoryl choline derivatives and/or non-cationic poly(meth)acrylates. The non-interactive polymer may be may fully or partially modified at or near the terminal end with reactive groups suitable for further functionalization (specifically OH, COOH, ester, SH, N-hydroxysuccinimidyl, maleimidyl, quinone and/or vinylsulfone groups); or fully or partially functionalized at or near the terminal end with a functional molecule which will specifically recognize and interact with target molecules (specifically a protein ligand, polynucleotide, carbohydrate or sugar ligand and/or simple organic molecules, especially biotin).

Preferred Substrates: (A) is of metal, metal oxide, inorganic material, organic material or charged polymer, specifically:

(i) negatively charged materials selected from oxides, nitrides, carbides or borides with isoelectric points below 9, polymers having a net negative charge and materials having a negative charge induced by surface pretreatment, especially tantalum, niobium, hafnium, silicon, iron or chromium oxides or iron, chromium, steel, tantalum, niobium, titanium, hafnium, gold or silver which carries a negative charge at the pH due to

the presence of native oxide films or charge inducing treatment; or (ii) positively charged materials selected from oxides with isoelectric points above 5, polymers having a net negative charge and oxides, metals or polymers having a positive charge induced by surface treatment at pH greater than 4, especially iron, chromium, steel, tantalum, niobium, titanium, hafnium, gold or silver which carries a positive charge at the pH due to the presence of native oxide films or charge inducing treatment.

L9 ANSWER 17 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-112499 [12] WPIDS
CR 2001-091751 [09]
DNC C2001-033517
TI Method for controlling the flux of penetrants across an adaptable semi-permeable barrier is useful for administering an agent to a mammalian body or a plant and for generating an immune response by vaccinating the mammal.
DC A18 A28 A96 B05 B07 D16 D22
IN CEVC, G; RICHARDSEN, H; WEILAND-WAIBEL, A; WEILAND-WEIBEL, A
PA (IDEA-N) IDEA AG
CYC 95
PI WO 2001001963 A1 20010111 (200112)* EN 110p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000061557 A 20010122 (200125)
BR 2000012178 A 20020312 (200226)
EP 1189598 A1 20020327 (200229) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CZ 2002000038 A3 20020515 (200241)
ADT WO 2001001963 A1 WO 2000-EP6367 20000705; AU 2000061557 A AU 2000-61557 20000705; BR 2000012178 A BR 2000-12178 20000705, WO 2000-EP6367 20000705; EP 1189598 A1 EP 2000-947939 20000705, WO 2000-EP6367 20000705; CZ 2002000038 A3 WO 2000-EP6367 20000705, CZ 2002-38 20000705
FDT AU 2000061557 A Based on WO 200101963; BR 2000012178 A Based on WO 200101963; EP 1189598 A1 Based on WO 200101963; CZ 2002000038 A3 Based on WO 200101963
PRAI WO 1999-EP4659 19990705
AB WO 200101963 A UPAB: 20020701
NOVELTY - A method for controlling the flux of penetrants across an adaptable semi-permeable porous barrier is new.

DETAILED DESCRIPTION - A method for controlling the flux of penetrants across an adaptable semi-permeable membrane comprises suspending the penetrants in a polar liquid in the form of fluid droplets surrounds by a membrane-like coating comprising at least two kinds of amphiphilic substances with a tendency to aggregate, selecting a dose of the penetrants to control the flux of the penetrants across the barrier and applying the selected dose of the formulation onto the area of the barrier. The amphiphilic substances differ by a factor of at least 10 in solubility in the polar liquid and the homo-aggregates of the more soluble substance and hetero-aggregates have a preferred average diameter smaller than the diameter of the homo-aggregates of the less soluble substance. The more soluble substance tends to solubilize the droplet and comprises up to 99% of the solubilizing concentration or saturating concentration in the unstabilized droplet. The presence of the more soluble substance lowers the average elastic energy of the coating by at least 5 times preferably more than 10 times the average elastic energy of red blood cells or of phospholipid bilayers with fluid aliphatic chains. The penetrants are able to transport agents through the pores of the barrier or enable agent permeation through the pores after the penetrants have

entered the pores.

INDEPENDENT CLAIMS are included for:

(i) a kit containing the formulation;

(ii) a patch containing the formulation; and

(iii) a method of administering an agent to a mammalian body or plant comprising the novel method.

USE - The method is useful for administering an agent to a mammalian body or a plant, for generating an immune response by vaccinating the mammal and for treating inflammatory disease, dermatosis, kidney or liver failure, adrenal insufficiency, aspiration syndrome, Behcet syndrome, bites and stings, blood disorders (cold-hemagglutinin disease), hemolytic anaemia, hypereosinophilic, hypoplastic anaemia, macroglobulinaemia and thrombocytopenic purpura), bone disorders, cerebral oedema, Cogan's syndrome, congenital adrenal hyperplasia, connective tissue disorders (lichen, lupus erythematosus, polymyalgia rheumatica, polymyositis and dermatomyositis), epilepsy, eye disorders (cataracts), Graves' ophthalmopathy, hemangioma, herpes infections, neuropathies, retinal vasculitis, scleritis, gastro-intestinal disorders (inflammatory bowel disease, nausea and oesophageal damage), hypercalcaemia, infections, Kawasaki disease, myasthenia gravis, pain syndromes, polyneuropathies, pancreatitis, respiratory disorders (asthma), rheumatoid disease, osteoarthritis, rhinitis, sarcoidosis, skin diseases, alopecia, eczema, erythema multiforme, lichen, pemphigus and pemphigoid, psoriasis, pyoderma gangrenosum, urticaria and thyroid and vascular disorders.

ADVANTAGE - Increasing the applied dose above a threshold level affects both the drug/penetrant distribution and also determines the rate of penetrant transport across the barrier.

Dwg.0/14

TECH UPTX: 20010302

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The flux is increased by enlarging the applied dose per area of the penetrants and the pH of the composition is preferably 3 to 10, especially 5 to 8. The formulation preferably comprises a thickening agent to raise the viscosity to maximally 5 Nm/s, especially 0.2Nm/s, an antioxidant to reduce the increase of oxidation index to less than 100% per 6 months, preferably 50% per 12 months and/or a microbicide to reduce the bacterial count after 4 days, preferably after 1 day, to less than 100/g for aerobic bacteria, less than 10 for entero-bacteria and less than 1 for Pseudomonas aeruginosa or Staphylococcus aureus. At least one microbicide is added in an amount that reduces the bacterial count of 1 million germs added per gram of total mass of the formulation after a period of 3 days and preferably after a period of 1 day. The thickening agent is selected from the class of pharmaceutically acceptable hydrophilic polymers, such as partially etherified cellulose derivatives, like carboxymethyl-, hydroxyethyl-, hydroxypropyl-, hydroxypropylmethyl- or methyl-cellulose; completely synthetic hydrophilic polymers such as polyacrylates , polymethacrylates, poly(hydroxyethyl)-, poly(hydroxypropyl)-, poly(hydroxypropylmethyl)methacrylates, polyacrylonitriles, methallyl-sulfonates, polyethylenes, polyoxyethylenes, polyethylene glycols, polyethylene glycol-lactides, polyethylene glycol-diacrylates, polyvinylpyrrolidones, polyvinyl alcohols, poly(propyimethacryimnides), poly(propylene fumarate-co-ethylene glycols), poloxamers, polyaspartamides, (hydrazine **cross-linked**) **hyaluronic acids**, silicones; natural gums comprising alginates, carrageenans, guar-gums, gelatins, tragacanths, (amidated) pectins, xanthans, chitosan collagens, agaroses; mixtures and further derivatives or co-polymers of them and / or other pharmaceutically, or at least biologically, acceptable polymers. The concentration of the polymer is in the range between 0.01 w- % and 10 w- %, more preferably in the range between 0. 1 w- % and 5 w- %, even more preferably in the range between 0.25 w- % and 3.5 w- % and most preferably in the range between 0.5 w- % and 2 w- %. The anti-oxidant is selected from synthetic phenolic anti-oxidants, such as butylated hydroxyanisol (BHA), butylated

hydroxytoluene
(BHT ) and di-tert-butylphenol (LY 178002, LY256548, HWA- 13 1, BF-389, Cl-
986, PD- 127443, E-5 119, BI-L-239XX, etc.), tertiary butylhydroquinone (TBHQ),
propyl gallate (PG), 1 -0-hexy)-2,3,5-trimethylhydroquinone (HTHQ); aromatic
**amines** (such as diphenylamine, p-alkylthio-o-anisidine, ethylenediamine derivatives, carbazol, tetrahydroindenoindol); phenols and phenolic acids (such as gualacol, hydroquinone, vanillin, gallic acids and their esters, protocatechuic acid, quinic acid, syringic acid, ellagic acid, salicylic acid, nordihydroguaiaretic acid (NDGA), eugenol; tocophenols (including tocophenols (alpha, beta, gamma, delta) and their derivatives, such as tocopheryl-acylate (e.g. -acetate, -laurate, myristate, -palmitate, -oleate, Ainoleate, etc., or any other suitable tocopheryl-lipoate), tocopheryl-POE-succinate; trolox and corresponding amide- and thiocarboxamide analogues; ascorbic acid and its salts, isoascorbate, (2 or 3 or 6)-o-alkylascorbic acids, ascorbyl esters (e.g. 6-o-lauroyl, myristoyl, paimitoyl-, oleoyl, or linoleoyi-L-ascorbic acid, etc.); non-steroidal anti-inflammatory agents (NSAIDs), such as indomethacin, diclofenac, mefenamic acid, flufenamic acid, phenylbutazone, oxyphenbutazone acetylsalicylic acid, naproxen, diflunisal, ibuprofen, ketoprofen, piroxicam, penicillamine, penicillamine disulphide, primaquine, quinacrine, chloroquine, hydroxychloroquine, azathioprine, phenobarbital, acetaminephen); aminosalicylic acids and derivatives; methotrexate, probucol, antiarrhytiunics (e.g. amiodarone, aprindine, asocainol), ambroxol, tamoxifen, b-hydroxytamoxifen; calcium antagonists (such as nifedipine, nisoldipine, nimodipine, nicardipine, nilvadipine), beta-receptor blockers (e.g. atenolol, propranolol, nebivolol); sodium bisulphite, sodium metabisulphite, thiourea; chelating agents, such as EDTA, GDTA, desferral; endogenous defence systems, such as transferrin, lactoferrin, ferritin, cearuloplasmin, haptoglobion, haemopexin, albumin, glucose, ubiquinol- 10; enzymatic antioxidants, such as superoxide dismutase and metal complexes with a similar activity, including catalase, glutathione peroxidase, and less complex molecules, such as beta-carotene, bilirubin, uric acid; flavonoids (e.g. flavones, flavonols, flavonones, flavanonals, chacones, anthocyanins), N-acetylcystein, mesna, glutathione, thiohistidine derivatives, triazoles; tannines, cinnamic acid, hydroxycinnamatic acids and their esters (e.g. cournaric acids and esters, caffeic acid and their esters, ferulic acid, (iso-) chlorogenic acid, sinapic acid); spice extracts (e.g. from clove, cinnamon, sage, rosemary, mace, oregano, allspice, nutmeg); carnosic acid, camosol, carsolic acid; rosmarinic acid, rosmarindiphenol, gentisic acid, ferulic acid; oat flour extracts, such as avenanthramide 1 and 2; thioethers, dithioethers, sulphoxides, tetralkylthiurarn disulphides; phytic acid, steroid derivatives (e.g. U74006F); tryptophan metabolites (e.g. 3-hydroxykynurenine, 3-hydroxyanthranilic acid), and organochalcogenides, or else is an oxidation suppressing enzyme. The concentration of BHA or BHT is between 0.001 and 2 w-% and especially between 0.005 and 0.02 w-%; of TBHQ and PG is between 0.001 and 2 w-%, most preferably is between 0.01 and 0.02 w-%; of tocopherols is between 0.005 and 5 w-%, most preferably is between 0.05 and 0.075 w-%; of ascorbic acid esters is between 0.001 and 5, most preferably is between 0.01 and 0.15 w-%; of ascorbic acid is between 0.001 and 5, most preferably is between 0.0 1 and 0.1 w-% of sodium bisulphite or sodium metabisulphite is between 0.001 and 5, most preferably is between 0.0 1 -0.15 w-%; of thiourea is between 0.0001 and 2 w-% and most preferably is between 0.001-0.01 w-% most typically 0.005 w-%; of cystein is between 0.01 and 5, most typically 0.5 w-%; of monothioglycerol is between 0.01 and 5 w-%, most typically 0.5 w-%; of NDGA is between 0.0005-2 w-% most typically 0.01 w-%; of glutathione is between 0.005 and 5 w-%, most typically 0. 1 w-%; of EDTA is between 0.00 1 and 5 w-%, most typically between 0.05 and 0.975 w-%; of citric acid is between 0.001 and 5 w-%, most typically between 0.3 and 2 w-%.

The microbicide is selected from short chain alcohols, such as ethyl and isopropyl alcohol, chlorbutanol, benzyl alcohol, chlorbenzyl alcohol, dichlorbenzylalcohol; hexachlorophene; phenolic compounds, such as cresol, 4-chloro-m-cresol, p-chloro-m-xylenol, dichlorophene, hexachlorophene, povidon-iodine; parabens, especially alkyl-paraben, such as methyl-, ethyl-, propyl-, or butyl-paraben, benzyl-paraben; acids, such as sorbic acid, benzoic acid and its salts; quaternary ammonium compounds, such as alkonium salts, e.g. benzalkonium salts, especially the chlorides or bromides, cetrimonium salts, e.g. the bromide; phenoalkeciniurn salt, such as phenododecinium bromide, cetylpyridinium chloride or other such salts; mercurium compounds, such as phenyImercuric acetate, borate, or nitrate, thiomersal; chlorhexidine or its gluconate; antibiotically active compounds of biological origin, or a mixture of it.
The bulk concentration of short chain alcohols in the case of ethyl, propyl, butyl or benzyl alcohol is up to 10 w-%, most preferably is in the range between 0.3-3 w-% and in the case of chlorobutanol is in the range between 0.3-0.6 w-% bulk concentration of parabens, especially in the case of methyl paraben is in the range between 0.05-0.2 w-% and in the case of propyl paraben is in the range between 0.002-0.02 w-% bulk concentration of sorbic acid is in the range between 0 .05-0.2 w-% and in the case of benzoic acid is in the range between 0. 1 -0.5 w-% bulk concentration of phenols, triclosan, is in the range between 0. 1-0.3 w-% and bulk concentration of chlorhexidine is in the range between 0.01-0.05 w-%.
The bulk concentration of short chain alcohols in the case of ethyl, propyl, butyl or benzyl alcohol is up to 10 w-%, most preferably is in the range between 0.3-3 w-% and in the case of chlorobutanol is in the range between 0.3-0.6 w-% bulk concentration of parabens, especially in the case of methyl paraben is in the range between 0.05-0.2 w-% and in the case of propyl paraben is in the range between 0.002-0.02 w-% bulk concentration of sorbic acid is in the range between 0 .05-0.2 w-% and in the case of benzoic acid is in the range between 0. 1 -0.5 w-% bulk concentration of phenols, triclosan, is in the range between 0. 1-0.3 w-% and bulk concentration of chlorhexidine is in the range between 0.01-0.05 w-%.
The less soluble amongst the aggregating substances is a lipid or lipid-like material, especially a polar lipid, whereas the substance which is more soluble in the suspending liquid and which lowers the average elastic energy of the droplet is a surfactant or else has surfactant-like properties and / or is a form of said lipid or lipid-like material which is comparably as soluble as said surfactant or the surfactant-like material.
The lipid or lipid-like material is a lipid or a lipoid from a biological source or a corresponding synthetic lipid or any of its modifications, the lipid preferably belonging to the class of pure phospholipids corresponding to the general formula where R1 and R2 is an aliphatic chain, typically a C10-20 acyl, or -alkyl or partly unsaturated fatty acid residue, in particular, an oleoyl-, palmitoeloyl-, elaidoyl-, linoleyl-, linolenyl-, linolenoyl-, arachidoyl-, vaccinyl-, lauroyl-, myristoyl-, palmitoyl-, or stearoyl chain; and where R3 is hydrogen, 2-trimethylamino-1-ethy 2-amino-1-ethyl, C 1-4-alkyl, C 1 -5-alkyl substituted with carboxy, C2-5-alkyl substituted with hydroxy, C2-5 -alkyl substituted with carboxy and hydroxy, or C2-5 alkyl substituted with carboxy and amino, inositol, sphingosine, or salts of said substances, said lipid comprising also glycerides, isoprenoid lipids, steroids, sterines or sterols, of sulphur- or carbohydrate-containing lipids, or any other bilayer-forming lipids, in particular half-protonated fluid fatty acids, said lipid is selected from the group comprising phosphatidylcholines, phosphatidylethanolamines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids, phosphatidylserines, sphingomyelins or other sphingophospholipids, glycosphingolipids (including cerebrosides, ceramidepolyhexosides, sulphatides, sphingoplasmalogens), gangliosides and other glycolipids or synthetic lipids, in particular with corresponding sphingosine derivatives, or any other glycolipids, whereby two similar or different chains can be

ester-groups-linked to the backbone (as in diacyl and dialkenoyl compound) ol be attached to the backbone with ether bonds, as in dialkyl-lipids. The surfactant or surfactant-like material is a nonionic, a zwitterionic, an anionic or a cationic surfactant, especially a fatty-acid or -alcohol, an alkyl-trildilmethyl-ammonium salt, an alkylsulphate salt, a monovalent salt of cholate, deoxycholate, glycocholate, glycodeoxycholate, taurodeoxycholate, taurocholate, etc., an acyl- or alkanoyl-dimethyl-aminoxide, esp. a dodecyl- dimethyl-aminoxide, an alkyl- or alkanoyl-N-methylglucamide, N- alkyl-NN- dimethylglycine, 3-(acyldimethylammonio)-alkanesulphonate, N-acyl- sulphobetaine, a polyethylene-glycol-octylphenyl ether, esp. a nonaethylene-glycol-octylphenyl ether, a polyethylene-acyl ether, esp. a nonaethylen-dodecyl ether, a polyethylene-glycol-isoacyl ether, esp. a octaethylene-glycol-isotridecyl ether, polyethylene-acyl ether, esp. octaethylenedodecyl ether, polyethylene- glycol-sorbitane-acyl ester, such as polyethylengiykol-20-monolaurate (Tween 20) or polyethylenglykol-20-sorbitan-monooleate (Tween 80), a polyhydroxyethylene- acyl ether, esp. polyhydroxyethylene- lauryl, -myristoyl, -cetylstearyl, or -oleoyl ether, as in polyhydroxyethylene-4 or 6 or 8 or 10 or 12, etc., -lauryl ether (as in Brij series), or in the corresponding ester, e.g. of polyhydroxyethylen-8-stearate (Myd 45), -laurate or -oleate type, or in polyethoxylated castor oil 40, a sorbitane- monoalkylate (e.g. in Arlacel or Span), esp. sorbitane-monolaurate, an acyl- or alkanoyl-N-methylgiucamide, esp. in or decanoyl- or dodecanoyl-N- methyIglucamide, an alkyl-sulphate (salt), e.g. in lauryl- or oleoyl-sulphate, sodium deoxycholate, sodium glycodeoxycholate, sodium oleate, sodium taurate, a fatty acid salt, such as sodium elaidate, sodium linoleate, sodium laurate, a lysophospholipid, such as n-octadecylene(=oleoyl)-glycerophosphatidic acid, - phosphorylglycerol, or -phosphorylserine, n-acyl-, e.g. lauryl or oleoyl-glycero- phosphatidic acid, -phosphorylglycorol, or -phosphorylserine, n-tetradecyl-glycero-phosphatidic acid, -phosphorylglycerol, or - phosphorylserine, a corresponding palmitoeloyP, elaidoyl-, vaccenyl-lysophospholipid or a corresponding short-chain phospholipid, or else a surface-active polypeptide.

The average diameter of the penetrant is preferably 30 to 500 nm, especially 60 to 150 nm and the total dry weight of the droplets is preferably 0.01 to 40%, especially 0.5 to 20%, of the formulation. The total dry weight of droplets in a formulation is selected to increase the formulation viscosity to maximally 200 mPas, especially up to 8 mPas. At least one amphiphilic substance and/or at least one edgeactive substance or surfactant, and/or at least one hydrophilic fluid and the agent are mixed, if required separately, to form a solution, the reulsting mixtures or solutions are then combined sbsequently to induce, preferably by action of mechanical energy such as shaking, stirring, vibrations, homogenisation, ultrasonication, shearing, freezing and thawing, or filtration using convenient driving pressure, the formation of penetrants that associate with and/or incorporate the agent. The amphilic substances are dissolved in volatile solvents, such as alcohols, especially ethanol, or in other pharmaceutically acceptable organic solvents, such as ethanol, 1- and 2-propanol, benzyl alcohol, propylene glycol, polyethylene glycol or glycerol, other pharmaceutically acceptable organic solvents, such as undercooled gas, especially supercritical carbon dioxide, which are then removed, especially by evaporation or dilution, prior to making the final preparation. The formation of the penetrants may be induced by the addition of required substances into a fluid phase, evaporation from a reverse phase, by injection or dialysis, if necessary under the influence of mechnical stress, such as shaking, stirring, in especially high velocity stirring, vibrating, homogenising, ultrasonication, shearing, freezing and thawing, or filtration using convenient, in especially low (1 MPa) or intermediate (up to 10 MPa), driving pressure. The formation of the penetrants may be induced by filtration, the filtering material having prores sizeds between 0.01microm and 0.8 microm, especially between 0.05

microm and 0.15 microm, where several filters may be used sequentially or in parallel. The agents and penetrants are made to associate, at least partly after the formation of the penetrants, e.g. after injecting a solution of the drug in a pharmaceutically acceptable fluid, such as ethanol, 1- and 2-propanol, benzyl alcohol, propylene glycol, polyethylene glycol or glycerol into the suspending medium and simultaneously with penetrant formation, if required using the drug co-solution and at least some, penetrant ingredients. The penetrants, with which the agent is associated, are prepared immediately before the application of the formulation, if convenient, from a suitable concentrate or a lyophylisate.
Preferred Kit: The kit comprises a device for administering a formulation contained in a bottle or any other packaging vessel.
Preferred Patch: The patch comprises a non-occlusive backing liner and an inner liner, where the backing liner and the inner liner define a reservoir and/or a matrix layer. The non-occlusive backing liner exhibits a mean vapor transmission rate (MVTR) of more than 1000 g/m squared day, preferably of more than 10.000 g/M squared day and has pores of smaller than 100 mn, preferably of smaller than 30 nm. The non-occlusive backing liner comprises a polyurethane membrane, preferably a polyester track-etched porous membrane, more preferably a polycarbonate track-etched porous membrane and most preferably a polyethylene microporous membrane. The inner liner prevents unwanted release of the formulation from the patch during storage and enables rapid skin wetting when contacted with the skin. the inner liner comprises a homogeneous membrane, preferably a polyester track-etched porous membrane or a polycarbonate track- etched. The membranes have a pore density of up to 5%, most preferably of more than 25% and/or a pore size in the range between 20 run and 200 nm, most preferably between 80 nm and 120 nm. The inner liner comprises a hydrophobic mesh-membrane and/or a nonwoven fleece with mesh openings formed by hydrophobic threads. The inner liner comprises a microporous polyethylene membrane having average pore sizes in the range of between 50 nm to 3000 nm, especially of about 1500 nm.
The patch comprises a pressure sensitive adhesive layer, preferably an adhesive layer comprising polyacylate, polyisobutylene, silicone, ethylene vinyl acetate copolymer, polyvinylpyrrolidone or polyethylene oxide hydrogel. The formulation viscosity is up to maximally 200 mPas, especially up to 8 mPas. The patch comprises one or more additional layers comprising desiccant containing layers, matrix layers, foam tape layers and/or protective layers. The patch comprises at least two compartments, which are separated from each other during storage. At least one of the compartments is inside and/or outside the patch. The formulation and/or the individual formulation components and/or the agent and/or the suspension/dispersion of penetrants without the agent are kept during the storage in several, preferably less than 5, especially in 2 separate compartments of the patch which, in case, are combined prior to or during or after the application of the patch. The outer compartment(s) comprise(s) injection systems, which are connected to the reservoir. The compartments are inside the reservoir, which is defined by the backing liner and the inner liner. The compartments are vertically stacked and /or are arranged side-by-side and / or one compartment is included in a second compartment, preferably without being fixed to the second compartment. The compartments are separated from each other by a controllably openable barrier, preferably a membrane and/or by a plug and/or by a compartment-forming lamination. Combining and mixing of the ingredients of the compartments is achieved by direct mechanical action, such as pressing, rubbing, kneading, twisting, tearing and /or indirectly by changing the temperature, osmotic pressure or electrical potential.

L9 ANSWER 18 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-102618 [11] WPIDS
DNC C2001-030011
TI Promotion of bone or cartilage tissue growth using injectable materials comprising a hyaluronic acid-linker-sulfated polysaccharide material which

can bind and release growth factors.

DC A11 A96 B04
IN LIU, L; SPIRO, R C
PA (ORQU-N) ORQUEST INC
CYC 94
PI WO 2000078356 A1 20001228 (200111)* EN 23p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000058778 A 20010109 (200122)
US 6288043 B1 20010911 (200154)
EP 1187636 A1 20020320 (200227) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SI
ADT WO 2000078356 A1 WO 2000-US16793 20000616; AU 2000058778 A AU 2000-58778 20000616; US 6288043 B1 US 1999-336005 19990618; EP 1187636 A1 EP 2000-944722 20000616, WO 2000-US16793 20000616
FDT AU 2000058778 A Based on WO 200078356; EP 1187636 A1 Based on WO 200078356
PRAI US 1999-336005 19990618
AB WO 200078356 A UPAB: 20010224

NOVELTY - A **hyaluronic acid** (HA), which is **cross-linked** through linking groups to a sulfated polysaccharide (SP), is used as an injectable composition for promoting bone or cartilage tissue growth. The linking groups are diamines or diamine-polyalkylene glycols.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) inducing growth of bone or cartilage tissue in vivo, by administering an injectable composition comprising (i) a composition as described above and (ii) a growth factor at the desired tissue growth site; and

(2) preparation of an injectable gel for supporting repair of bone or cartilage, comprising: (i) oxidizing HA to form a modified HA containing aldehyde groups; (b) reacting the modified HA with a linking agent containing terminal **amine** groups to form a HA with pendant linking groups and terminal **amine** groups; and (c) reacting this HA with a modified SP containing aldehyde groups, to covalently link the SP to the linking groups.

ACTIVITY - Osteopathic.

The effect of hyaluronate-heparin imine-linked (HAHPi) gels, which contained FGF-2, on periosteal bone formation, was examined in Sprague-Dawley rats (4-6 weeks old; 140-160 g; male). 50 micro l aliquots of gel formulations containing FGF-2 (10 ng-1 mg/ml), or control carrier solution, were injected into pockets created under the periosteum of the parietal bone of the rats. The animals were sacrificed after 14 days and the thickness of the parietal bone, excluding the thickness of the periosteum, was examined. The mean thickness of the parietal bone was (i) 660 micro m for rats treated with a HAHPi/FGF-2 gel, (ii) 294 micro m for rats treated with a FGF-2/buffer formulation, (iii) 283 micro m for rats treated with a HA/FGF-2 formulation and (iv) 309 micro m for rats treated with HAHPi alone.

MECHANISM OF ACTION - None given.

USE - The injectable composition is useful for inducing tissue growth at a target bone or cartilage site. It can be used for filling of bone defects, for fracture repair or for grafting periodontal defects.

ADVANTAGE - Growth factors are capable of binding specifically to the gels and being released by the gels. This release occurs in a controlled manner that is dependent on the density of the gel. The HA component chiefly imparts the property of making the composition injectable and retainable at the site of desired tissue growth.

Dwg.0/5

TECH UPTX: 20010224
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: the composition is a water-soluble, viscous gel. The SP is heparin, chondroitin sulfate, dextran sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, hexuronyl hexosaminoglycan sulfate, inositol hexasulfate or sucrose octasulfate. The linking group is ethylene diamine, hexane diamine, dodecane diamine or diamine-polyethylene glycol. The molecular weight of the linking group is 1000-6000 Daltons. The molecular weight of the HA is 1 x 106 to 2 x 106 Daltons. The molecular weight of the SP is less than 104 Daltons. The HA is bonded to the linking group by an amine, while the SP is bonded to the linking group by an amine or imine. The composition can be prepared as described in (2) above. The composition may also comprise a growth factor e.g. an insulin-like growth factor, transforming growth factor-beta, bone morphogenic protein, epidermal growth factor and especially a fibroblast growth factor.

L9 ANSWER 19 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-587131 [55] WPIDS
CR 1998-130292 [12]
DNN N2000-434554 DNC C2000-174979
TI Medical devices, comprising a polymer having both ionic and nonionic crosslinks, has improved mechanical properties and shape memory and is useful in biliary, urinary or vascular stents and tissue prosthesis.
DC A11 A14 A25 A26 A96 B07 D16 D22 P32 P34
IN GODSHALL, D E; MADENJIAN, A R; RONAN, J M; THOMPSON, S A; ZHONG, S P; PING, S Z; RONAN, J A
PA (SCIM-N) SCIMED LIFE SYSTEMS INC
CYC 22
PI WO 2000050103 A1 20000831 (200055)* EN 43p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 2000035037 A 20000914 (200063)
US 6368356 B1 20020409 (200227)
ADT WO 2000050103 A1 WO 2000-US4937 20000225; AU 2000035037 A AU 2000-35037 20000225; US 6368356 B1 Cont of US 1996-679609 19960711, Provisional US 1999-122176P 19990225, Provisional US 1999-122256P 19990225, CIP of US 2000-496709 20000202, US 2000-512698 20000225
FDT AU 2000035037 A Based on WO 200050103; US 6368356 B1 Cont of US 6060534, CIP of US 6184266
PRAI US 1999-122256P 19990225; US 1999-122176P 19990225; US 1996-679609 19960711; US 2000-496709 20000202; US 2000-512698 20000225
AB WO 200050103 A UPAB: 20020429
NOVELTY - A medical device having a shape memory comprises a polymer having both ionic and nonionic crosslinks.
USE - The devices are useful as biliary, urinary or vascular stents and tissue prosthesis.
ADVANTAGE - The hydrogel polymers provide improved mechanical properties so that the devices are more easily inserted into or removed from the body.
Dwg.0/5
TECH UPTX: 20001102
TECHNOLOGY FOCUS - BIOLOGY - The medical device may further include a radiopaque filler and the polymer is preferably **hyaluronic acid**, heparin, chondroitin sulphate, pectinic acid, a carboxyl-derivatised polysaccharide and/or a synthetic polymer (polyhydroxy ethyl methacrylate, polyvinyl alcohol, polyacrylamide, poly(N-vinyl pyrrolidone), polyethylene oxide, hydrolysed polyacrylonitrile, polyacrylic acid, polymethacrylic acid, polyethylene **amine** and/or a polysaccharide (alginic acid, pectinic acid, carboxymethyl cellulose, **hyaluronic acid**, chitosan, polyvinyl alcohol, chitosan, cationic guar, cationic starch or polyethylene **amine**)). It is preferably conformable to the shape of a stent, catheter, cannula, plug, filler, constrictor, bone anchor,

plate, rod, seed, sheet or tube and may be seeded with cells. It may include an additive (antiseptic, antibiotic, anticoagulant, contraceptive, nucleic acid (gene, cDNA, vector, RNA, antisense molecule, ribozyme or PNA molecule), protein or medicine) for medical treatment and an additive for mechanical property adjustment. The non-ionic bonds are preferably covalent **crosslinking** bonds and the **crosslinks** may be distributed homogeneously or heterogeneously. The polymer may be dissolvable and different portions may dissolve at different rates and the device may contain a non-dissolvable polymer (silicone, polyethylene oxide and/or polyvinyl alcohol) which may be in the form of a string or mesh. The device may include at least one pigtail end.

L9 ANSWER 20 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-411505 [35] WPIDS
DNC C2000-124563
TI New **crosslinked hyaluronic acids** are useful as substitutes for synovial fluid or vitreous humor, as controlled-release matrices, as healing and antiadhesive agents and in vascular prosthesis.
DC A96 B03 B07 D21 D22
IN BARBUCCI, R; RAPUOLI, R
PA (AQUI-N) AQUISITIO SPA; (FALO-N) FALORNI ITAL FARM SRL
CYC 91
PI WO 2000027887 A2 20000518 (200035)* EN 22p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000026600 A 20000529 (200041)
BR 9915235 A 20010724 (200147)
NO 2001002315 A 20010706 (200151)
CZ 2001001650 A3 20010912 (200158)
EP 1144459 A2 20011017 (200169) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
IT 1303735 B 20010223 (200214)
CN 1328573 A 20011226 (200227)
KR 2001101001 A 20011114 (200230)
HU 2001004296 A2 20020328 (200234)
ADT WO 2000027887 A2 WO 1999-EP8481 19991108; AU 2000026600 A AU 2000-26600 19991108; BR 9915235 A BR 1999-15235 19991108, WO 1999-EP8481 19991108; NO 2001002315 A WO 1999-EP8481 19991108, NO 2001-2315 20010510; CZ 2001001650 A3 WO 1999-EP8481 19991108, CZ 2001-1650 19991108; EP 1144459 A2 EP 1999-968778 19991108, WO 1999-EP8481 19991108; IT 1303735 B IT 1998-MI2440 19981111; CN 1328573 A CN 1999-813143 19991108; KR 2001101001 A KR 2001-705929 20010510; HU 2001004296 A2 WO 1999-EP8481 19991108, HU 2001-4296 19991108
FDT AU 2000026600 A Based on WO 200027887; BR 9915235 A Based on WO 200027887; CZ 2001001650 A3 Based on WO 200027887; EP 1144459 A2 Based on WO 200027887; HU 2001004296 A2 Based on WO 200027887
PRAI IT 1998-MI2440 19981111
AB WO 200027887 A UPAB: 20000725
NOVELTY - **Crosslinked hyaluronic acids** obtained by reaction of the carboxylic acids with a **polyamine** are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(i) complexes of zinc, copper or iron and the **crosslinked hyaluronic acid**;
(ii) use of **crosslinked hyaluronic acids** and complexes as substitutes for synovial fluid or vitreous humor, as controlled-release matrices and as healing and antiadhesive agents;
(iii) use of **crosslinked hyaluronic acids**

in vascular prosthesis, biohybrid organs, healing devices, ophthalmic and otological compositions, prosthesis, implants and medical devices;

(iv) biomaterials comprising the **crosslinked hyaluronic acids**.

USE - The **crosslinked hyaluronic acids** are useful as substitutes for synovial fluid (for the treatment of osteoarthritic conditions) or vitreous humor, as artificial tears for the treatment of dry eye conditions, as controlled-release matrices, as wound or skin ulcer healing devices and antiadhesive agents for artificial blood vessels and heart valves. , in vascular prosthesis, biohybrid organs, ophthalmic products (lens substitutes and contact lenses) and otological compositions. They are generally applicable in various anti-adhesion implants for use in surgery and in medical devices such as stents, catheters and cannulas and in biomaterials. The **crosslinked hyaluronic acids** are also useful as moisturizing agents, as bases for cosmetic formulations and as injectable filling agents.

ADVANTAGE - The **cross-linked hyaluronic acids** have high biocompatibility, high resistance to enzymatic degradation (especially after sulfation), high capacity to absorb water and ability to chelate metal ions.

Dwg.0/0

TECH UPTX: 20000725

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The **polyamine** is preferably a diamine, especially of formula R1NH-A-NHR2

A = 2-10C alkylene (optionally substituted by OH, carboxy, halo, alkoxy or NH2), ((CH2)n-O-(CH2)n)m, aryl or heteroaryl;

n = 2 or 3;

m = 2 to 10;

R1, R2 = H, 1-6C alkyl, phenyl or benzyl.

The **crosslinked hyaluronic acids** may be sulfated or hemisuccinylated.

L9 ANSWER 21 OF 34 WPIDS (C) 2002 THOMSON DERWENT

AN 2000-387405 [33] WPIDS

DNC C2000-117538

TI Preparation of **crosslinked** polysaccharides containing carboxy groups by activation of carboxy groups by reacting with carboxy-activating groups in anhydrous protic solvent and then with **polyamine**.

DC A11 A96 B07 D21

IN BARBUCCI, R; SPORTOLETTI, G

PA (AQUI-N) AQUISITIO SPA

CYC 91

PI WO 2000027886 A1 20000518 (200033)* EN 27p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000013803 A 20000529 (200041)

BR 9915238 A 20010724 (200147)

NO 2001002316 A 20010706 (200151)

EP 1137670 A1 20011004 (200158) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

CZ 2001001651 A3 20011212 (200206)

IT 1303738 B 20010223 (200214)

CN 1325409 A 20011205 (200223)

KR 2001101002 A 20011114 (200230)

HU 2001004075 A2 20020429 (200238)

ADT WO 2000027886 A1 WO 1999-EP8480 19991109; AU 2000013803 A AU 2000-13803

19991109; BR 9915238 A BR 1999-15238 19991109, WO 1999-EP8480 19991109; NO 2001002316 A WO 1999-EP8480 19991109, NO 2001-2316 20010510; EP 1137670 A1 EP 1999-971819 19991109, WO 1999-EP8480 19991109; CZ 2001001651 A3 WO 1999-EP8480 19991109, CZ 2001-1651 19991109; IT 1303738 B IT 1998-MI2443 19981111; CN 1325409 A CN 1999-813144 19991109; KR 2001101002 A KR 2001-705930 20010510; HU 2001004075 A2 WO 1999-EP8480 19991109, HU 2001-4075 19991109

FDT AU 2000013803 A Based on WO 200027886; BR 9915238 A Based on WO 200027886; EP 1137670 A1 Based on WO 200027886; CZ 2001001651 A3 Based on WO 200027886; HU 2001004075 A2 Based on WO 200027886

PRAI IT 1998-MI2443 19981111

AB WO 200027886 A UPAB: 20000712

NOVELTY - Processes for the preparation of **crosslinked** polysaccharides containing carboxy groups comprising:

(a) activation of the carboxy groups of the polysaccharide by reaction with suitable carboxy-activating groups in anhydrous protic solvent; and

(b) reaction of the carboxy-activated polysaccharide with a **polyamine**.

USE - The processes are used to prepare **crosslinked** polysaccharides containing carboxy groups (claimed), which are used in the medical, pharmaceutical, veterinary and dermo-cosmetic fields.

ADVANTAGE - The processes provide a high degree of reproducibility of the obtained products in terms of **crosslinking** degree, homogeneity of the distribution of the **crosslinking** chains and chemico-physical characteristics of the products and the technological characteristics of the articles obtained from the products, which are important for the medical, pharmaceutical and dermo-cosmetic fields. The **crosslinked** carboxylated polysaccharides can be prepared in a wide range of shapes characterized by different properties such as viscoelasticity, hydration degree, complexing ability towards metal ions, ability to form hydrogels, moldability in films or sponges and mechanical strength of the final materials.

Dwg.0/0

TECH UPTX: 20000712

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Preparation: The polysaccharide is a **hyaluronic acid** (obtained from tissues or bacteria), carboxymethyldextran, carboxymethylcellulose, carboxymethylstarch, alginic acids, cellulosic acid, N-carboxymethyl or butyl glycans or chitosans, heparins with different molecular weights, optionally desulfated and succinylated, dermatan sulfates, chondroitin sulfates, heparan sulfates or polyacrylic acids. The carboxy-activating agent is carbonyldiimidazole, carbonyltriazole, chloromethylpyridylium iodide, hydroxybenzotraizole, p-nitrophenol, p-nitrophenyltrifluoroacetate or N-hydroxysuccinimide. The **polyamines** are of formula (I), polyoxyalkylene chains of formula (II), aryl or hetaryl, preferably 1,3- or 1,4-disubstituted benzene. The polysaccharide is salified with lipophilic cations, preferably tributyl or tetralkyl ammonium. The **crosslinking** reaction is carried out in anhydrous dimethylformamide or tetrahydrofuran. The obtained **crosslinked** polysaccharide is further subjected to sulfation of the hydroxy groups by reaction with the pyridine/sulfur trioxide complex. The sulfation reaction is carried out in dimethylformamide in a heterogeneous phase at 0-10degreesC for 0.5-6 hours. The **crosslinked**, optionally sulfated polysaccharide is further subjected to complexation reaction with aqueous solutions of copper, zinc or iron ions.

R1, R2 = H, 1-6C alkyl, phenyl or benzyl;

A = 2-10 (2-6)C alkylene chain optionally substituted by hydroxy, carboxyl, halo, alkoxy or amino;

n = 2-3; and

m = 2-10.

L9 ANSWER 22 OF 34 WPIDS (C) 2002 THOMSON DERWENT

AN 2000-303127 [26] WPIDS
CR 2000-292769 [24]
DNN N2000-226533 DNC C2000-091848
TI New hydrogel compositions useful for drug delivery or as temporary tissues scaffolds, comprises cross-linked hyaluronic acid derivatives.
DC A11 A96 B04 B07 D16 D22 P34
IN AESCHLIMANN, D; BULLPITT, P; BULPITT, P
PA (AESC-I) AESCHLIMANN D; (BULP-I) BULPITT P; (ORTH-N) ORTHOGENE LLC
CYC 89
PI WO 2000016818 A1 20000330 (200026)* EN 63p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 9961922 A 20000410 (200035)
EP 1115433 A1 20010718 (200142) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000016818 A1 WO 1999-EP6913 19990917; AU 9961922 A AU 1999-61922 19990917; EP 1115433 A1 EP 1999-948783 19990917, WO 1999-EP6913 19990917
FDT AU 9961922 A Based on WO 200016818; EP 1115433 A1 Based on WO 200016818
PRAI US 1998-156829 19980918
AB WO 200016818 A UPAB: 20000531
NOVELTY - New **crosslinked** hyaluronic compositions useful as hydrogels for controlled delivery of drugs and as tissue scaffolds.

DETAILED DESCRIPTION - A composition comprising a **hyaluronic acid** derivative comprising disaccharide subunits where at least 1 of the disaccharide units has a substitution at a carboxyl group so that it is of formula (I) is new.

R', R'' = side chains containing functional groups (H, bioactive peptide, alkyl, aryl, alkylaryl; arylalkyl substituted alkylaryl containing O, N, S or P; or substituted arylalkyl containing O, N, S, P, halo or a metal atom) bound directly to each other or separated by keto, ether, amino, oxycarbonyl, sulfate, sulfoxide, carboxamide, alkyne or alkene groups. The side chain terminates with H, peptide, aldehyde, **amine**, arylazide, hydrazide, maleimide, sulfhydryl, optionally active ester, carboxylate, imidoester, halo or OH groups.

INDEPENDENT CLAIMS are included for:

(1) a composition comprising a **hyaluronic acid** ester of formula (II);

(2) hydrogels containing **crosslinked hyaluronic acid** derivatives of formulae (I) or (II);

(3) preparation of **hyaluronic acid** derivatives comprising:

(a) forming an activated ester on a carboxylate of a glucuronic acid group of **hyaluronic acid**;

(b) substituting at the carbonyl carbon of the activated ester with a side chain comprising a nucleophilic portion and a functional group portion; and

(c) optionally forming a **crosslinked** hydrogel from the product;

(4) forming a matrix for a temporary scaffold for tissue repair from the product of (c) above, where either:

(a) the **crosslinker** is a polyvalent active ester, an aldehyde, an **amine**, an arylazide, maleimide or sulfhydryl; or

(b) the **hyaluronic acid** derivative is **crosslinked** using transglutaminase;

(5) tissue adhesives comprising either:

(a) the hydrogel of (2) where the side chain is an activated ester, aldehyde, arylazide or maleimide;

(b) (II);

(c) a hydrogel of (2) where the **crosslinked** hyaluronic derivative is formed using a polyvalent active ester, aldehyde, arylazide or maleimide as **cross-linker**; or

(d) a hydrogel of (2) where the hydrogel is formed in the presence of growth factors, cytokines, drugs and/or bioactive peptides;

(6) matrices for cell structures comprising either:

(a) a hydrogel of (2) where either the **crosslinked** **hyaluronic acid** derivatives are formed as is (5) (c)

(b) a hydrogel as in (2) which is formed as in (5)(d);

(c) a hydrogel as in (2).

R = substituted triazole, N-sulfosuccinimide, nitrophenol, partially halogenated phenol or pentafluorophenol.

USE - The compositions are especially used for the controlled delivery of bioactive agents such as drugs, cytokines , growth factors and cells. The hydrogels are used as temporary scaffolds for tissue regeneration in e.g. cartilage repair. They may be used to promote bone repair, treat pathological wound conditions such as chronic ulcers, as scaffolds to generate artificial tissues or organ (e.g. skin or liver), to generate tissue separation or to prevent tissue adhesion following surgery, for tissue augmentation in plastic surgery.

ADVANTAGE - The methods allow versatile modification of **hyaluronic acid** allowing for **crosslinking** under physiological conditions, but do not compromise its molecular weight or chemical identity.

Dwg.0/13

TECH UPTX: 20000531

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: In the composition containing (I), at least 5 % and at most 95 % of the disaccharide subunits are substituted. Alternatively, at most 5 % of the disaccharide subunits are substituted. At least 1 of the terminal functional groups is a peptide an aldehyde, an **amine**, an arylazide, a hydrazide, a maleimide, a sulfhydryl or an active ester and the composition can be **crosslinked**. The molecular weight of the composition is either: at least 100000 Da; at most 100000 Da; or at least 1000000 Da; and is water soluble.

Preferred Hydrogel: The hydrogel is biodegradable.

Preferred Method: In the preparation of the **hyaluronic acid** derivative, the nucleophilic portion is ammonia, primary or secondary **amine**, OH or sulfhydryl. Step (a) is performed with an active ester, especially N-sulfosuccinimide, substituted triazole, nitrophenol, partially halogenated phenol, perhalophenol, pentafluorophenol, HOBT or NHS, by carbodiimide mediated coupling. Step (c) is carried out in the presence of cells, growth factors (especially TGF-beta or BMP) cytokines, drugs and/or bioactive peptides (especially RGD or APQQEA), especially in situ in a patient in need of tissue repair

L9 ANSWER 23 OF 34 WPIDS (C) 2002 THOMSON DERWENT

AN 2000-194969 [17] WPIDS

DNC C2000-060377

TI Use of hyaluronic acid and its derivatives for treatment of ulcers, lesions and diverticula of the digestive tract and for reconstruction of digestive tract.

DC A96 B04 D22

IN AMBROSIO, L; CALLEGARO, L; ESPOSITO, A; ESPOSITO, A C

PA (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL

CYC 87

PI WO 2000001394 A1 20000113 (200017)* EN 22p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

AU 9949053 A 20000124 (200027)
EP 1096940 A1 20010509 (200128) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
IT 1300286 B 20000503 (200206)
JP 2002519381 W 20020702 (200246) 25p
ADT WO 2000001394 A1 WO 1999-EP4604 19990702; AU 9949053 A AU 1999-49053 19990702; EP 1096940 A1 EP 1999-932791 19990702, WO 1999-EP4604 19990702; IT 1300286 B IT 1998-PD168 19980706; JP 2002519381 W WO 1999-EP4604 19990702, JP 2000-557840 19990702
FDT AU 9949053 A Based on WO 200001394; EP 1096940 A1 Based on WO 200001394; JP 2002519381 W Based on WO 200001394
PRAI IT 1998-PD168 19980706
AB WO 200001394 A UPAB: 20000405
NOVELTY - Use of hyaluronic acid or its derivatives for preparation of a composition for treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) use of a bi- or three-dimensional matrix comprising at least one hyaluronic acid compound as a support for cellular growth for the preparation of biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus.

(2) a biological material comprising:

(a) intestinal cells optionally together with fibroblasts, mesenchymal cells mature cells and/or epithelial cells;

(b) a 3-dimensional or bi-dimensional matrix comprising at least one hyaluronic compound.

ACTIVITY - Antiulcer.

MECHANISM OF ACTION - None given.

USE - For treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus. The compositions are useful for the reconstruction of the wall of the digestive apparatus.

No relevant example demonstrating these activities is given.

ADVANTAGE - The compositions are biodegradable and biocompatible.

Dwg.0/8

TECH UPTX: 20000405
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: The **hyaluronic acid** derivative is:
(A) an ester where part or all of the carboxy functions are esterified with aliphatic, aromatic, arylaliphatic, cycloaliphatic or heterocyclic alcohols or with alcohols of the same polysaccharide chain or other chains;
(B) a **crosslinked hyaluronic acid** compound where some or all of the carboxy functions are esterified with aliphatic, aromatic, arylaliphatic, cycloaliphatic or heterocyclic poly-alcohols;
(C) a hemiester of succinic acid (optionally in the form of a heavy metal salt) with **hyaluronic acid** or its esters;
(D) an O- or N-sulfated derivative;
(E) an amide where some or all of the free carboxylic acid groups are reacted with aliphatic, aromatic, arylaliphatic, cycloaliphatic or heterocyclic primary or secondary **amines**;
(F) an amide where a deacylated amino group of **hyaluronic acid** is reacted with an aliphatic, aromatic, arylaliphatic or cycloaliphatic acid.
Preferred Composition: The composition further comprises pharmacologically or biologically active substances comprising antibiotics (preferably active against Helicon pylori), growth factors, antimicotics, antimicrobials and/or antiviral agents.
Preferred Matrix: The 3-dimensional matrix is a non-woven fabric and the bi-dimensional matrix is a perforated membrane.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Cells - The cells are mature, mesenchymal, epithelial and/or fibroblasts.

L9 ANSWER 24 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-072523 [06] WPIDS
DNN N2000-056756 DNC C2000-020712
TI Treating premature rupture of membranes during pregnancy to extend degree of fetal maturity.
DC A96 B07 P31
IN ENSCORE, D J; HERMAN, S J; KABLIK, J J; KAZO, G M
PA (FOCA-N) FOCAL INC; (BIEN-I) BIENIARZ A
CYC 87
PI WO 9960938 A1 19991202 (200006)* EN 37p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9940948 A 19991213 (200020)
EP 1079749 A1 20010307 (200114) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6350463 B1 20020226 (200220)
AU 745302 B 20020321 (200233)
JP 2002516140 W 20020604 (200239) 40p
ADT WO 9960938 A1 WO 1999-US11352 19990521; AU 9940948 A AU 1999-40948 19990521; EP 1079749 A1 EP 1999-924451 19990521, WO 1999-US11352 19990521; US 6350463 B1 Provisional US 1998-86624P 19980523, US 1999-316879 19990521; AU 745302 B AU 1999-40948 19990521; JP 2002516140 W WO 1999-US11352 19990521, JP 2000-550406 19990521
FDT AU 9940948 A Based on WO 9960938; EP 1079749 A1 Based on WO 9960938; AU 745302 B Previous Publ. AU 9940948, Based on WO 9960938; JP 2002516140 W Based on WO 9960938
PRAI US 1998-86624P 19980523; US 1999-316879 19990521
AB WO 9960938 A UPAB: 20000203
NOVELTY - Treating premature rupture of membranes in pregnancy (PROM) comprises:

(a) applying a fluent material to a tissue from at least one of an amniotic membrane (3), a cervix (2) and a uterine wall (1); and

(b) causing the fluent material to become a non-fluent material.

The non-fluent material completely seal the tissue to retain the amniotic fluid.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a device for treating PROM comprising a proximal end for manipulation of the device, a distal end for insertion into the patient's body, and at least one lumen with an opening at the distal end of the device suitable for delivery of a fluent material.

USE - The method is used for treating premature rupture of the membranes in pregnancy for extending the degree of fetal maturity. It prevents or minimizes the fluid leakage. It can be used to seal the small incisions necessary for a surgery and also simplifies fetal surgery. It allows surgical opening of the membranes, e.g. in a caesarian section, to allow open surgery to be performed on the fetus

ADVANTAGE - The fluent material is biocompatible and non-toxic (claimed).

DESCRIPTION OF DRAWING(S) - The figure shows a schematic diagram of a gravid uterus.

Uterine wall 1
Cervix 2
Amniotic membrane 3
Abdominal wall 4
Transabdominal access route 5

Dwg.1/1

TECH UPTX: 20000203
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: The fluent material that becomes non-fluent, forms a seal at the membrane or

uterine wall and (b) is induced by one or more processes from a change in temperature, photoinitiation of **crosslinking**, chemical induction of **crosslinking**, spontaneous covalent **crosslinking**, ionic **crosslinking**, change in ionic strength or composition, change in pH, coacervation, and precipitation induced by change in solvent polarity. The method further comprises applying a material to the tissue which increases the adherence of the seal to the tissue, inserting a partially preformed barrier or sealant material and sealing a surgical incision in at least one of an amniotic membrane and uterine wall of a pregnant patient by delivering a fluent material to the surgical incision. The method comprises inserting at least one of a sheath and tube into the vagina and placing a treatment device in at least one of the sheath and tube. The method includes accessing a treatment site of a uterine wall, amniotic membrane, or cervix of a patient percutaneously; and treating the treatment site.
Preferred Device: The device contains at least one addition element from a source of electromagnetic radiation or other activator of polymerization; a second lumen for injection of a primer; a channel for removal of excess primer by vacuum or flushing, which may be the same as the primer application channel; a visualization device, which may be an endoscope or a hysteroscope; a partially or completely preformed barrier device; and markers to allow verification of the instrument's position, e.g. by ultrasound. It further comprises one or more devices for temporary occlusion of the cervix to prevent backflow of applied materials or to stop amniotic fluid efflux during formation of a hydraulic barrier. The temporary occlusion device is selected from an inflatable balloon, a mechanical occlusion device, and a swellable device. The device may also have a cervical sleeve, adapted for transvaginal insertion into the distal cervix and a sheath for lining a passage created via a transabdominal incision.

TECHNOLOGY FOCUS - POLYMERS - Preferred Materials: The non-fluent material forming the hydraulic seal has a tensile strength to withstand a pressure of 30 cm of water without loss of adherence. The non-fluent material comprises a hydrogel formed from the fluent material by gelatinization or **crosslinking**. The fluent material includes a therapeutic agent.
The seal is at least partially on the fetal side of the amniotic membrane. The gelling material is one or more of a natural material, including agarose, alginate, pectin, xanthan, carrageenan, konjac glucomannan, **hyaluronic acid**, collagen, and gelatin; and a synthetic material comprising a polymeric backbone bearing reactive groups. The backbone is polysaccharides, polyamides, polyesters, polyorthoesters, polycarbonates, polyalkylene oxides, polylactones, poly(n-vinyl) compounds, such as polyvinylpyrrolidone, poly(meth)acrylates (i.e., polyacrylates or polymethacrylates or their copolymers), polyvinyl acetate and polyvinyl alcohol, polyanhydrides, silicones, and their copolymers. The reactive group is free-radical polymerizable groups, such as (meth)aryl, allyl, vinyl, fumaryl, maleyl, and other ethylenically-unsaturated groups; urethane-forming pairs (isocyanates with **amines**); and epoxides with **amines** or alcohols.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Agent: The agent is selected from tocolytics, antibiotics, bacteriostats, contrast agents for sonography, radiography, or MRI, growth factors for promoting healing of the membranes, and hemostatic agents.

L9 ANSWER 25 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 1999-370731 [31] WPIDS
DNN N1999-276442 DNC C1999-109376
TI Increasing nucleic acid synthesis by ultrasonic treatment of cells.
DC A96 B04 D16 P33
IN MCCREERY, T; SADEWASSER, D; UNGER, E C
PA (IMAR-N) IMARX PHARM CORP

CYC 21
PI WO 9925385 A1 19990527 (199931)* EN 123p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9913906 A 19990607 (199943)
ADT WO 9925385 A1 WO 1998-US23843 19981111; AU 9913906 A AU 1999-13906 19981111
FDT AU 9913906 A Based on WO 9925385
PRAI US 1997-971540 19971117
AB WO 9925385 A UPAB: 19990806
NOVELTY - Increasing synthesis of nucleic acid (I) in a cell by exposing it to ultrasound is new.
DETAILED DESCRIPTION - (I) is:
(a) an endogenous sequence (Ia) encoding a stress or repair protein, or
(b) an introduced exogenous sequence (Ib).
INDEPENDENT CLAIMS are also included for the following:
(1) method for identifying (I) showing increased synthesis following application of ultrasound;
(2) method for changing expression of (Ia) by applying ultrasound; and
(3) method for causing expression of (Ib) by applying ultrasound.
ACTIVITY - Anticancer. A patient with a malignant melanoma was treated with 1.5 mg plasmid DNA containing a cytomegalovirus promoter and c-fos upstream of the interleukin-2 (IL-2) gene, combined with cationic phospholipids at lipid:DNA ratio 1:6. Injection was directly into a metastasis in the retroperitoneum and 24 hr later ultrasonic imaging was performed with subsequent application of focused high-intensity ultrasound (1.5 MHz at 2 W/cm2) for 60 seconds. This treatment increased intratumoral synthesis of IL-2 and reduced the tumor mass.
MECHANISM OF ACTION - Modulation of gene expresion.
USE - The method is specifically used therapeutically:
(i) to treat phenylketonuria (following introduction of (Ib) for phenylalanine hydroxylase);
(ii) to increase expression of the p53 tumor suppressor;
(iii) to increase production of IL-2, particularly associated with natural killer cells, and
(iv) for treating cancer by administering a sequence antisense to initiation factor 3 and/or tRNA synthase.
More generally, (Ib) may include one or more genes or fragments, or even complete chromosomes, for delivery (in vivo, in vitro or ex vivo) to animal or plant cells for treating a very wide range of conditions, e.g. acquired immune deficiency syndrome, autoimmune diseases, chronic viral infections; hemophilia, cystic fibrosis, cancer.
ADVANTAGE - Ultrasonic treatment increases expression of (I) and increases uptake of (Ib), particularly of 4-6 kb.
Dwg.0/2
TECH UPTX: 19990806
TECHNOLOGY FOCUS - BIOLOGY - Preferred Proteins: (Ia) may encode e.g. initiation factor 3, tRNA synthase, a heat shock protein (particularly hsp 27, 89a or 60), ubiquinone oxidreductase, XP-A, B, C or G nucleotides excision repair gene proteins, beta-polymerase, ubiquitin, catalase. (Ib) may encode a proto-oncogene, or a stress, repair or structural protein, e.g. those specified for (Ia), Ras, c-fos, c-myc.
Preferred Process: (Ib) is administered to the cell, with, after or before application of ultrasound, which is in the range 5-40 (especially about 25) kHz. (I) may be RNA or DNA, particularly in an animal (specifically human) or plant cell, and synthesis of (I) is measured by reverse transcription polymerase chain reaction (RT-PCR). Ultrasound is applied for 5-120 (preferably 30) seconds. (Ib) is administered together with an organic halide (II), as gas, liquid or gaseous precursor (converted to gas by ultrasound), particularly a perfluorocarbon or perfluoroether compound, but also sulfur or selenium hexafluorides. About 80 (II) are listed,

particularly preferred are perfluorohexane and perfluorocyclohexane. In presence of (II), ultrasound frequency is 40 kHz to 25 MHz with energy level 0.5-10 W/square cm, at 200-500 kHz (0.2-0.5 W/square cm) or 1-20 MHz (0.1-0.2 W/cm2). Ultrasound is applied at a duty cycle of 1-100 (preferably 10-20)% of the treatment time. The (Ib)/(II) combination may be formulated with a carrier, particularly a polymer, cationic **polyamine**, protein or lipid, or a metal ion, e.g. calcium, magnesium or zinc. About 100 carriers are specified, e.g. dioleoylphosphatidylethanolamine (DOPE), sphingomyelin, gangliosides GM1 or 2, poly(ethylene glycol) of molecular weight 2, 5 or 8 kDa, chitin, **hyaluronic acid**, poly(vinyl pyrrolidone), poly(ethyleneimine), cholesterol sulfate or hemisuccinate, or their mixtures, optionally formulated as vesicles. The carrier may also include a ligand for targeting selected cells. The process may be carried out in vivo, in vitro or ex vivo.
Preferred Treatment: Ultrasound is delivered from a portable device, particularly one worn by the patient, and is activated either manually or automatically at predetermined intervals.

TECHNOLOGY FOCUS - PHARMACEUTICALS - To treat phenylketonuria, (Ib) encoding phenylalanine hydroxylase (PAH) is administered in a solid, porous matrix of 1:3 DPEPC (dipalmitoylethyl-phosphatidylcholine) and DOPE, also containing perfluorohexane and the PAH-encoding plasmid. A similar matrix is used to deliver the sequence encoding p53. To deliver a sequence encoding interleukin-2, the porous solid matrix contains DMRIE (dimyristoyloxypropyl-3-dimethyl(hydroxyethyl)ammonium bromide) and DOPE.

L9 ANSWER 26 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 1995-336736 [43] WPIDS
DNC C1995-148451
TI New active ester(s) of carboxy-polysaccharide(s) or their derivs. - with e.g. (hetero)-aromatic alcohol, are intermediates for amide etc. derivs., used in tissue repair and for controlled release of peptide(s).
DC A11 A96 B04 D22
IN BELLINI, D; RIGHETTO, Z
PA (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL
CYC 20
PI WO 9524429 A1 19950914 (199543)* EN 42p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 749446 A1 19961227 (199705) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
IT 1268955 B 19970318 (199740)
US 5856299 A 19990105 (199909)
EP 749446 B1 19991124 (199954) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69513507 E 19991230 (200007)
ES 2141925 T3 20000401 (200023)
ADT WO 9524429 A1 WO 1995-EP932 19950313; EP 749446 A1 EP 1995-913099 19950313, WO 1995-EP932 19950313; IT 1268955 B IT 1994-PD43 19940311; US 5856299 A WO 1995-EP932 19950313, US 1996-702673 19961126; EP 749446 B1 EP 1995-913099 19950313, WO 1995-EP932 19950313; DE 69513507 E DE 1995-613507 19950313, EP 1995-913099 19950313, WO 1995-EP932 19950313; ES 2141925 T3 EP 1995-913099 19950313
FDT EP 749446 A1 Based on WO 9524429; US 5856299 A Based on WO 9524429; EP 749446 B1 Based on WO 9524429; DE 69513507 E Based on EP 749446, Based on WO 9524429; ES 2141925 T3 Based on EP 749446
PRAI IT 1994-PD43 19940311
AB WO 9524429 A UPAB: 19951102
Active esters (I) of a carboxypolysaccharide (II) or its semisynthetic deriv. are new. At least some COOH gps. are esterified with (hetero)aromatic alcohol (opt. substd.) and/or N-hydroxy-**amine**.
If not fully esterified, the remaining COOH gps. are salified by quat.

ammonium, alkali and/or alkaline earth metal cations. Also claimed are (1) the following amide derivs. of **hyaluronic acid** (HA):
(a) N-ethylamide with 10% COOH as amide and 90% as Na salt; (b) N-benzylamide with 50% COOH as amide and 50% as Na salt; (c) amide deriv. with 100% COOH amidified with Arg; (d) peptide deriv. with 50% COOH esterified with ethanol, 25% COOH converted to amide with the fibronectin inhibitor H-Arg-Gly-Asp-OH (III) and 25% as Na salt; and (e) peptide deriv. of the benzyl ester of **hyaluronic acid** p75 with the peptide inhibitor of fibrinolysis H-Gly-Pro-Arg-OH (IV) with 75% COOH esterified with benzyl alcohol and 25% COOH as amide with the peptide; and (2) any modified (II) produced from (I).

USE - (I) are intermediates for modified (II), esp. esters, thioesters and amides. (I) and modified (II) are useful for biomedical and pharmaceutical appplications, e.g. in cosmetics, health care or surgical articles (e.g. microcapsules, microspheres, threads, films, gauzes and sponges) or diagnostic kits (partic. to derivatise solid surfaces for coupling proteins, for use in assays or cell/tissue culture plate). Partic. uses are in tissue repair and for controlled release of biologically active amino acid, peptide and protein.

ADVANTAGE - (I) have high reactivity; good selectivity for **amines** over OH and SH gps., are stable and easy to store. They can be prepd. without **crosslinking** side reactions. Amides prepd. from (I) are more stable than corresponding esters so provide slow, controlled release of attached peptide, etc.
Dwg.0/0

L9 ANSWER 27 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 1995-182988 [24] WPIDS
DNC C1995-084902
TI Crosslinking hyaluronic acid deriv. - using carbodiimide or di- or polyepoxy cpd., used in slow-release formulations and for forming composites with reinforcing materials or high mol. drugs.
DC A11 A96 B04
PA (GNZE) GUNZE KK; (KAKE) KAKEN PHARM CO LTD
CYC 1
PI JP 07102002 A 19950418 (199524)* 6p
ADT JP 07102002 A JP 1993-245072 19930930
PRAI JP 1993-245072 19930930
AB JP 07102002 A UPAB: 19950626
Method for **crosslinking hyaluronic acid** (HA) comprises adding carbodiimide (CDI) or a di- or poly-epoxy cpd. to an aq. soln. of HA, and drying the soln.

Also claimed are (A) a **crosslinked hyaluronic acid** obtained by treating **hyaluronic acid** at 37deg.C in phosphate buffer salt (PBS) for 2-30 days; (B) a **crosslinked hyaluronic acid** complex contg. a biodegradable reinforcing material (I); and (C) a slow-release material for a biologically-active material (II) which contains (II) in **crosslinked** HA.

Pref. HA is reacted with CDI using HA aq. soln. of pH 4-8 in a mixt. of an organic solvent and water in ratio 60-100; 40-0 (by wt.) at 4-45deg.C.

The solvent opt. contains a basic **amine** acid or its methyl or ethyl ester. Excess CDI is converted to urea.

USE - The **crosslinked** HA and composites are materials for medical treatment.

The composite may be a film or multilayer with a material (I) such as polylactic acid, such as heparin, or an antibiotic or antimicrobial (I) and be used to treat thrombosis, prevent adhesions, promote heating and control injections.
Dwg.0/0

L9 ANSWER 28 OF 34 WPIDS (C) 2002 THOMSON DERWENT

AN 1993-329469 [42] WPIDS
CR 1995-178828 [23]
DNC C1993-145636
TI Water-swellable, water-insol. modified polysaccharide - obtd. by forming a mixt. of water-soluble modified polysaccharide, water and a **crosslinking** agent, recovering the polysaccharide and heat treating the prod..
DC A11 A96 D22 F07 P34
IN QIN, J
PA (KIMB) KIMBERLY CLARK CORP; (KIMB) KIMBERLY-CLARK WORLDWIDE INC; (KIMB) KIMBERLY-CLARK CORP
CYC 13
PI EP 566118 A1 19931020 (199342)* EN 20p
R: BE DE ES FR GB IT NL SE
AU 9336949 A 19931021 (199349)
CA 2076732 A 19931018 (199403)
JP 06025303 A 19940201 (199409) 13p
AU 9654638 A 19960801 (199638)
AU 673158 B 19961031 (199651)
EP 566118 B1 19970917 (199742) EN 22p
R: BE DE ES FR GB IT NL SE
DE 69313908 E 19971023 (199748)
ES 2107574 T3 19971201 (199803)
AU 690844 B 19980430 (199829)
MX 187502 B 19971217 (199936)
KR 244422 B1 20000201 (200118)
EP 566118 B2 20011017 (200169) EN
R: BE DE ES FR GB IT NL SE
JP 3221963 B2 20011022 (200169) 14p
ADT EP 566118 A1 EP 1993-106150 19930415; AU 9336949 A AU 1993-36949 19930415; CA 2076732 A CA 1992-2076732 19920824; JP 06025303 A JP 1993-56262 19930317; AU 9654638 A Div ex AU 1993-36949 19930415, AU 1996-54638 19960531; AU 673158 B AU 1993-36949 19930415; EP 566118 B1 EP 1993-106150 19930415; DE 69313908 E DE 1993-613908 19930415, EP 1993-106150 19930415; ES 2107574 T3 EP 1993-106150 19930415; AU 690844 B Div ex AU 1993-36949 19930415, AU 1996-54638 19960531; MX 187502 B MX 1993-1563 19930319; KR 244422 B1 KR 1993-4776 19930326; EP 566118 B2 EP 1993-106150 19930415; JP 3221963 B2 JP 1993-56262 19930317
FDT AU 673158 B Previous Publ. AU 9336949; DE 69313908 E Based on EP 566118; ES 2107574 T3 Based on EP 566118; AU 690844 B Previous Publ. AU 9654638; JP 3221963 B2 Previous Publ. JP 06025303
PRAI US 1992-870529 19920417
AB EP 566118 A UPAB: 20011126
Method comprises: forming a mixt. comprising a water-soluble modified polysaccharide, water and a **cross-linking** agent; recovering the modified polysaccharide from the mixt.; and heat treating the prod. at above 80 deg.C to **crosslink** and render it water insol. Also claimed is the polysaccharide produced.

Pref. the modified polysaccharide is selected from a carboxylated, sulphonated, sulphated or phosphated derivs. of polysaccharides and/or their salts (esp. carboxyalkyl cellulose, mor esp. carboxymethyl cellulose). The **crosslinking** agent is an organic cpd. comprising at least two functional gps. capable of reacting with a carboxyl or hydroxyl gp. of a polysaccharide (esp. diamines, **polyamines**, diols and/or polyols, more esp. chitosan glutamate, type of gelatin, diethylenetriamine, ethylene glycol, butylene glycol, polyvinyl alcohol, **hyaluronic acid**, polyethylene imine and/or their derivs.. The recovered modified polysaccharide is heat-treated to cause **cross-linking** or the **crosslinking** involves self-**crosslinking** through esterification. When the **crosslinking** agent is a diamine or **polyamine**, the recovered modified polysaccharide is heat-treated to cause **crosslinking** formed by esterification and amidation.

USE/ADVANTAGE - The polysaccharide produced has good absorption properties similar to the synthetic highly absorptive materials and is suitable for use in personal care absorbent prods. such as diapers, training pants and feminine care prods..
Dwg.0/3

L9 ANSWER 29 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 1993-182688 [22] WPIDS
CR 1991-325347 [44]; 1994-150866 [18]
DNN N1993-140406 DNC C1993-080972
TI Contrast medium for diagnostic imaging - comprises gel particles of less than 90 microns in mean dia. and which comprise a polymer entrapping a contrast enhancing metal.
DC A96 B04 P31 S03 S05
IN UNGER, E C
PA (UNGE-I) UNGER E C; (IMAR-N) IMARX PHARM CORP
CYC 20
PI WO 9310440 A1 19930527 (199322)* EN 43p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE
W: AU CA JP
AU 9228940 A 19930615 (199340)
EP 614527 A1 19940914 (199435) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE
US 5358702 A 19941025 (199442) 13p
JP 07501331 W 19950209 (199515)
AU 667491 B 19960328 (199622)
US 5976500 A 19991102 (199953)
ADT WO 9310440 A1 WO 1992-US8948 19921020; AU 9228940 A AU 1992-28940 19921020; EP 614527 A1 EP 1992-922870 19921020, WO 1992-US8948 19921020; US 5358702 A CIP of US 1990-507125 19900410, Cont of US 1991-794437 19911119, US 1993-62325 19930514; JP 07501331 W WO 1992-US8948 19921020, JP 1993-509251 19921020; AU 667491 B AU 1992-28940 19921020; US 5976500 A CIP of US 1990-507125 19900410, Cont of US 1991-794437 19911119, Div ex US 1993-62325 19930514, US 1994-285977 19940804
FDT AU 9228940 A Based on WO 9310440; EP 614527 A1 Based on WO 9310440; JP 07501331 W Based on WO 9310440; AU 667491 B Previous Publ. AU 9228940, Based on WO 9310440; US 5976500 A Div ex US 5358702
PRAI US 1991-794437 19911119; US 1990-507125 19900410; US 1993-62325 19930514; US 1994-285977 19940804
AB WO 9310440 A UPAB: 19991215
Contrast medium comprises gel particles of less than 90 microns in mean diameter. The gel particles comprise a polymer entrapping a contrast enhancing metal.

Also claimed are (1) a contrast medium of gel particles which comprise a non-**crosslinked** polymer entrapping a contrast enhancing metal; (2) a method of providing an image of an internal region of a patient, or for diagnosing the presence of diseased tissue in a patient, comprises: (i) administering to the patient a contrast medium as described in (A) or (B) above, and (ii) scanning the patient using magnetic resonance imaging, ultrasound imaging X-ray imaging to obtain visible images of the region or of any diseased galacturonans, glucans, mannans, xylans, levan, fucoidan, carrageenan, galactocarolose, pectins, pectic acids, amylose, pullulan, glycogen, amylopectin, cellulose, dextran, pustulan, chitin, agarose, keratin, chondroitin, dermatan, **hyaluronic acid**, alginic acid, xanthan gum, starch, carboxymethyl cellulose, hydroxymethylcellulose, hydroxypropylmethylcellulose, methylcellulose, methoxycellulose, and polysaccharides contg. an aldose, ketose, acid or **amine** selected from erythrose, threose, ribose, arabinose, xylose, lyxose, allose, altrose, glucose, mannose, gulose, idose, galactose, tabose, erythrulose, ribulose, xylulose, psicose, fructose, sorbose, tagatose, glucuronic acid, gluconic acid, glucanic acid, galacturonic acid, mannuronic acid, glucosaminae galactosamine and neuraminic acid. Pref. the polysaccaride is

pectin which is a low methoxy pectin having phosphorylated 30% methoxylation, polygalacturonic acid or the polymer may be a phosphorylated polymer
Dwg.0/1
Dwg.0/1

L9 ANSWER 30 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 1992-415455 [50] WPIDS
CR 1989-099990 [13]; 1991-171108 [23]; 1996-299900 [30]
DNC C1992-184342
TI Water insol. polyanionic polysaccharide derivs. - prepd. by reacting with activating agent and opt. nucleophile, useful e.g. to prevent tissue adhesion after surgery and for sustained drug delivery.
DC A96 B07 P34
IN BURNS, J W; MILLER, R; XU, X; MILLER, R J
PA (GENZ) GENZYME CORP; (MILL-I) MILLER R J; (XUXX-I) XU X
CYC 21
PI WO 9220349 A1 19921126 (199250)* EN 46p
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU CA FI JP NO
AU 9221434 A 19921230 (199313)
EP 587715 A1 19940323 (199412) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
JP 06508169 W 19940914 (199441)
EP 587715 A4 19950809 (199618)
AU 670030 B 19960704 (199634)
AU 9652267 A 19960801 (199638)
US 5760200 A 19980602 (199829)
US 6030958 A 20000229 (200018)
US 6174999 B1 20010116 (200106)
US 6235726 B1 20010522 (200130)#
US 2001039336 A1 20011108 (200171)
EP 1229050 A2 20020807 (200259) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
ADT WO 9220349 A1 WO 1992-US4212 19920519; AU 9221434 A AU 1992-21434 19920519, WO 1992-US4212 19920519; EP 587715 A1 EP 1992-912424 19920519, WO 1992-US4212 19920519; JP 06508169 W WO 1992-US4212 19920519, JP 1993-500263 19920519; EP 587715 A4 EP 1992-912424 ; AU 670030 B AU 1992-21434 19920519; AU 9652267 A Div ex AU 1992-21434 19920519, AU 1996-52267 19960513; US 5760200 A CIP of US 1987-100104 19870918, CIP of US 1990-543163 19900625, CIP of US 1991-703254 19910520, Div ex US 1992-833973 19920211, US 1995-377949 19950125; US 6030958 A CIP of US 1987-100104 19870918, CIP of US 1990-543163 19900625, Cont of US 1991-703254 19910520, Cont of US 1994-176334 19940103, Cont of US 1994-326058 19941019, US 1997-914320 19970818; US 6174999 B1 CIP of US 1987-100104 19870918, CIP of US 1990-543163 19900625, CIP of US 1991-703254 19910520, US 1992-833973 19920211; US 6235726 B1 CIP of US 1987-100104 19870918, CIP of US 1990-543163 19900625, Div ex US 1997-914320 19970818, US 1999-376266 19990818; US 2001039336 A1 CIP of US 1987-100104 19870918, CIP of US 1990-543163 19900625, CIP of US 1991-703254 19910520, Cont of US 1992-833973 19920211, US 2001-757202 20010109; EP 1229050 A2 Div ex EP 1992-912424 19920519, EP 2002-7980 19920519
FDT AU 9221434 A Based on WO 9220349; EP 587715 A1 Based on WO 9220349; JP 06508169 W Based on WO 9220349; AU 670030 B Previous Publ. AU 9221434, Based on WO 9220349; US 5760200 A CIP of US 4937270, CIP of US 5017229; US 6030958 A CIP of US 4937270, CIP of US 5017229; US 6174999 B1 CIP of US 4937270, CIP of US 5017229; US 6235726 B1 CIP of US 4937270, CIP of US 5017229, Div ex US 6030958; US 2001039336 A1 CIP of US 4937270, CIP of US 5017229, Cont of US 6174999; EP 1229050 A2 Div ex EP 587715
PRAI US 1992-833973 19920211; US 1991-703254 19910520; US 1987-100104 19870918; US 1990-543163 19900625; US 1995-377949 19950125; US 1994-176334 19940103; US 1994-326058 19941019; US 1997-914320

19970818; US 1999-376266 19990818; US 2001-757202 20010109

AB WO 9220349 A UPAB: 20020916

Water-insol. biocompatible compsn. (A) is made by mixing, in aq. medium, at least one polyanionic polysaccharide (I); a nucleophile (II) and an activating agent (III). Opt. the reaction mixt. also includes a modifying agent (N) able to form new active carbonyl gps. on (I). Also new are (I) (A) themselves and (2) a similar process (or products) using only (I) and (II).

Pref. (I) is carboxymethylcellulose (CMC), carboxymethylamylose (CMA), **hyaluronic acid** (HA), chondroitin-6-sulphate, dermatin sulphate, heparin or heparin sulphate, esp. a mixt. of CMC or CMA with HA. (III) is a hexafluorophosphate or halide salt of benzotriazol-1-yloxytris (dimethylamino) phosphonium; O-benzotriazol-1-yl N,N,N',N'-tetramethylauronium; or bromotris(NM12 or pyrrolidinyl)phosphonium; or it is a carbodiimide, esp. 1-ethyl-3-(dimethylamino propyl)carbodiimide (EDC) or its methiodide. (II) is an aminoacid (or ester, amide or salt); monofunctional **amine**; amino-alcohol, thiol, -phenol or catechol; peptide or protein; a pref. example is a lysine ester. Suitable (N) include 1-hydroxybenzotriazole hydrate, N-hydroxysuccinimide, 2- or 4-nitro(thio)phenol; imidazole, etc. (V) is esp. a protein, growth factor, enzyme, drug, biopolymer or biologically compatible synthetic polymer. In the reaction medium, the (I) concn. is 0.0002-0.1 (pref. 0.005-0.02)M and reaction is at pH 3.5-8, depending on the nature of (III). At least 0.1 mole equiv. (III) and at least 1 mole equiv. (II) are reacted per mole equiv. (I).

USE/ADVANTAGE - (A) have reduced water solubility without requiring **crosslinking** agents, so can be washed with water or organic solvents to remove any unreacted material. Retain their strength even when hydrated and adhere to tissue without sutures, even in presence of bleeding. (A) can be coloured to facilitate handling. Compsns. are partic. used as post-operative adhesion-preventing membranes but many other potential applications include surface pacification; as sealants in anastomotic sites for catheters; vascular grafts, prosthetic devices which require sealing of potential leakage sites; as sclerosing agents; tissue replacements or sustained release drug delivery systems.

Dwg.0/0

L9 ANSWER 31 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 1992-315909 [38] WPIDS
CR 1992-315907 [38]; 1992-315908 [38]; 1992-315910 [38]; 1996-209173 [21]
DNC C1992-140312
TI Bio-adhesive liposome(s) - covalently linked to gelatin, collagen or hyaluronic acid, for use as a microscopic drug delivery system.
DC B05 B07
IN MARGALIT, R
PA (BAXT) BAXTER INT INC
CYC 18
PI WO 9214447 A1 19920903 (199238)* EN 18p
RW: BE CH DE DK ES FR GB GR IT LI LU NL SE
W: AU CA JP
AU 9190370 A 19920915 (199251)
EP 525132 A1 19930203 (199305) EN 18p
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
JP 05505827 W 19930826 (199339) 5p
AU 651414 B 19940721 (199432)
US 5401511 A 19950328 (199518) 4p
EP 525132 B1 19960103 (199606) EN 10p
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
DE 69116144 E 19960215 (199612)
ES 2084335 T3 19960501 (199625)
ADT WO 9214447 A1 WO 1991-US8113 19911030; AU 9190370 A AU 1991-90370 19911030, WO 1991-US8113 19911030; EP 525132 A1 WO 1991-US8113 19911030, EP 1992-900243 19911030; JP 05505827 W WO 1991-US8113 19911030, JP

1992-500899 19911030; AU 651414 B AU 1991-90370 19911030; US 5401511 A Cont of US 1991-655878 19910214, US 1992-960196 19921009; EP 525132 B1 WO 1991-US8113 19911030, EP 1992-900243 19911030; DE 69116144 E DE 1991-616144 19911030, WO 1991-US8113 19911030, EP 1992-900243 19911030; ES 2084335 T3 EP 1992-900243 19911030

FDT AU 9190370 A Based on WO 9214447; EP 525132 A1 Based on WO 9214447; JP 05505827 W Based on WO 9214447; AU 651414 B Previous Publ. AU 9190370, Based on WO 9214447; EP 525132 B1 Based on WO 9214447; DE 69116144 E Based on EP 525132, Based on WO 9214447; ES 2084335 T3 Based on EP 525132

PRAI US 1991-655878 19910214; US 1992-960196 19921009

AB WO 9214447 A UPAB: 19971030

Modified liposomes comprise a liposome component covalently linked to 'a non growth factor recognising substance component' (sic).

Liposomes are covalently linked to gelatin, collagen or hyaluronic acid to obtain 'bioadhesive' liposomes potentially useful for drug delivery.

Liposomes contg. phosphatidylethanolamine (PE) are incubated with gelatin, collagen or hyaluronic acid in the presence of a crosslinking agent, esp. glutaraldehyde (GAD) or a water-soluble carbodiimide (esp. EDC).

The liposomes are pref. multilamellar vesicles (MLV), microemulsified liposomes (MEL) or large unilamellar vesicles (LUVET).

ADVANTAGE - Liposomes offer potential advantages as a microscopic drug delivery system

Dwg.0/0

L9 ANSWER 32 OF 34 WPIDS (C) 2002 THOMSON DERWENT

AN 1992-048266 [06] WPIDS

CR 1993-367850 [46]; 1994-183228 [22]; 1997-020305 [02]

DNN N1992-036715 DNC C1992-021547

TI Prepn. of biocompatible surface modified materials - by covalently grafting a polymeric material using radio frequency plasma induction.

DC A35 A96 D22 P32

IN KAMEL, I; SOLL, D B

PA (OPHT-N) OPHTHALMIC RES CORP; (UYDR-N) UNIV DREXEL

CYC 2

PI US 5080924 A 19920114 (199206)*

ZA 9308318 A 19950125 (199510)# 24p

ADT US 5080924 A US 1989-342270 19890424; ZA 9308318 A ZA 1993-8318 19931108

PRAI US 1989-342270 19890424; ZA 1993-8318 19931108

AB US 5080924 A UPAB: 19970115

Permanent modification of a substrate surface comprises: a polymeric, biocompatible material (I) is covalenty grafted onto the surface by radio frequency (TF) plasma induction. (I) has pendant terminal carboxylic acid or **amine** gps..

Grafting is pref-induced in an RF plasma reactor generating a freq of 1-40 esp ca 13.56 MHz, pref in the presence of N2, NH3 or esp Ar. Pref. (I) are ethylenediamine, diethylenetriamine, or allylamine pref polyacrylic acid (all esp initially as monomers). Pref. substrates are silicone, polypropylene, polyester, polytetrafluoroethylene, polyurethane, hydroxyethylmethacrylate, or esp. polymethylmethacrylate.

The surface may be further modified by covalently **cross-linking** a 2nd biocompatible material (II) to the grafted (I) using a **cross-linking** agent (III) (pref. applied before (II)). (II) is pref a polysaccharide, esp. **hyaluronic acid**, hyaluronate, agarose, or partic chondroitin sulphate. (III) is pref. bis(3,5-dibromosalicyl)fumarate, 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide, esp glutaraldehyde. The substrate is pref. rinsed with distilled H2O before **cross-linking** (II), and the **cross-linking** is pref. effected in the presence of a neutral buffer soln.

ADVANTAGE - The method affords a microscopically smooth, biocompatible surface, and is esp useful in prepg biocompatible

prostheses, partic intraocular lenses for mammals. @(8pp Dwg.No.0/0)@

L9 ANSWER 33 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 1989-334101 [46] WPIDS
CR 1994-281158 [35]
DNN N1989-254138 DNC C1989-148067
TI Crosslinked carboxy acidic polysaccharide cpds. - contg. carboxyl gps. crosslinked by ester bonding or lactonic bonding to hydroxyl gps. of polysaccharide(s).
DC A11 A96 A97 B07 D14 D21 P34
IN DELA, VALLE F; ROMEO, A; DELLAVALLE, F; DELLA, VALLE F; DELLA-VALLE, F; ROMAEO, A
PA (FIDI-N) FIDIA SPA; (FIDI-N) FIDIA FARM ITAL DER
CYC 23
PI EP 341745 A 19891115 (198946)* EN
R: AT CH DE ES FR GB GR IT LI LU NL SE
WO 8910941 A 19891116 (198948) EN 9p
W: AU DK FI HU JP KR
AU 8935747 A 19891129 (199007)
FI 9000188 A 19900112 (199012) 12p
DK 9000109 A 19900312 (199035)
HU 53666 T 19901128 (199102)
JP 02504163 W 19901129 (199103)
IT 1219587 B 19900518 (199213)
EP 341745 B1 19941214 (199503) EN 30p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 68919900 E 19950126 (199509)
ES 2064378 T3 19950201 (199511)
NZ 229100 A 19950828 (199540)
HU 210926 B 19950928 (199545)
IL 90274 A 19960912 (199644)
CA 1339122 C 19970729 (199742)
US 5676964 A 19971014 (199747) 22p
JP 10324701 A 19981208 (199908) 26p
JP 2941324 B2 19990825 (199940) 25p
FI 107050 B1 20010531 (200137)
ADT WO 8910941 A WO 1989-EP519 19890512; JP 02504163 W JP 1989-505458 19890512; IT 1219587 B IT 1988-47964 19880513; EP 341745 B1 EP 1989-108630 19890512; DE 68919900 E DE 1989-619900 19890512, EP 1989-108630 19890512; ES 2064378 T3 EP 1989-108630 19890512; NZ 229100 A NZ 1989-229100 19890512; HU 210926 B HU 1989-3636 19890512, WO 1989-EP519 19890512; IL 90274 A IL 1989-90274 19890512; CA 1339122 C CA 1989-599557 19890512; US 5676964 A Cont of US 1989-350919 19890512, Cont of US 1993-70505 19930601, US 1995-465055 19950605; JP 10324701 A Div ex JP 1989-505458 19890512, JP 1998-152832 19890512; JP 2941324 B2 JP 1989-505458 19890512, WO 1989-EP519 19890512; FI 107050 B1 WO 1989-EP519 19890512, FI 1990-188 19900112
FDT DE 68919900 E Based on EP 341745; ES 2064378 T3 Based on EP 341745; HU 210926 B Previous Publ. HU 53666, Based on WO 8910941; JP 2941324 B2 Previous Publ. JP 02504163, Based on WO 8910941; FI 107050 B1 Previous Publ. FI 9000188
PRAI IT 1988-47964 19880513
AB EP 341745 A UPAB: 20010704
(A) **Cross-linked** carboxy acidic polysaccharides are claimed in which at least a first portion of the carboxyl gps. of the polysaccharide are **cross-linked** by ester bonding or lactonic bonding to hydroxyl gps. of the same polysaccharide molecule and/or to hydroxyl gps. of different polysaccharide molecules.

The polysaccharide may be e.g. **hyaluronic acid**, alginic acid, CMC or carboxymethylchitin. A second portion of carboxyl gps. of the polysaccharide may be esterified with a mono- or polyvalent alcohol, e.g. ethyl alcohol, octyl alcohol, ethylene glycol, glycolic acid, alkaloids, phenylethyl **amines**, phenothiazine drugs, thioxanthene drugs or sulphamidics. (B) Also claimed are salts of the

**cross-linked** polysaccharides of (A) with an alkaline or alkaline earth metal or an **amine** e.g. alkaloids, phenothiazine, benzodiazepine, thioxanthene, hormones or vitamins.

(C) Also claimed is a process for the prepn. of **crosslinking** carboxy acidic polysaccharides which comprises (a) teating an acidic polysaccharide with an activating agent to activate the carboxy gps., and (b) subjecting the intermediate activated polysaccharide derivs. to heat or irradiation. The activating agent may be a carbodiimide, ethoxyacetylene, Woodward's reagent or chloroacetonitryl. It may be a chloride of 2-chloro-N-methyl-pyridine and reacts with a tetrabutylammonium salt of the polysaccharide in the presence of a tert. **amine** base. The process may be carried out in an organic aprotic solvent, e.g. DMSO.

USE - The new **cross-linked** prods. esterified with therapeutically active alcohols and/or salified with therapeutically active bases are therapeutically more efficacious and have a greater and/or longer-lasting effect as compared to the starting drugs. The **cross-linked** polysaccharides can also be used in the alimentary, cosmetic, sanitary and surgical fields, in the prodn. of paper, resin, dye and household goods.

0/0

L9 ANSWER 34 OF 34 WPIDS (C) 2002 THOMSON DERWENT
AN 1989-099990 [13] WPIDS
CR 1991-171108 [23]; 1992-415455 [50]; 1996-299900 [30]
DNC C1989-044177
TI Water insoluble biocompatible hyaluronic acid gel - prepd. by activating hyaluronic acid with e.g. carbodiimide and reaction with nucleophile.
DC B04 P34
IN ACHARYA, R A; FOX, E M; HAMILTON, R G; WATTS, A E; WALTS, A E; ACHARYA, R
PA (GENZ) GENZYME CORP
CYC 18
PI WO 8902445 A 19890323 (198913)* EN 24p
RW: AT BE CH DE FR GB IT LI NL SE
W: AU DK FI JP NO
AU 8824825 A 19890417 (198929)
FI 9001330 A 19900316 (199022)
NO 9001229 A 19900514 (199025)
US 4937270 A 19900626 (199028)
DK 9000689 A 19900517 (199031)
EP 397652 A 19901122 (199047)
R: AT BE CH DE FR GB IT LI LU NL SE
JP 03502704 W 19910620 (199131)
NO 9402763 A 19900316 (199435)
CA 1332235 C 19941004 (199440)
FI 94357 B 19950515 (199525)
EP 397652 B1 19960605 (199627) EN 11p
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3855351 G 19960711 (199633)
JP 09183804 A 19970715 (199738) 7p
JP 2670996 B2 19971029 (199748) 7p
JP 2684208 B2 19971203 (199802) 7p
NO 301770 B1 19971208 (199805)
NO 309001 B1 20001127 (200065)
ADT WO 8902445 A WO 1988-US2969 19880826; US 4937270 A US 1987-100104 19870918; EP 397652 A EP 1988-908557 19880826; JP 03502704 W JP 1988-507745 19880826; NO 9402763 A WO 1988-US2969 19880826, Div ex NO 1990-1229 19900316, NO 1994-2763 19940722; CA 1332235 C CA 1988-577623 19880916; FI 94357 B WO 1988-US2969 19880826, FI 1990-1330 19900316; EP 397652 B1 EP 1988-908557 19880826, WO 1988-US2969 19880826; DE 3855351 G DE 1988-3855351 19880826, EP 1988-908557 19880826, WO 1988-US2969 19880826; JP 09183804 A Div ex JP 1988-507745 19880826, JP 1996-357953 19880826; JP 2670996 B2 Div ex JP 1988-507745 19880826, JP 1996-357953

19880826; JP 2684208 B2 JP 1988-507745 19880826, WO 1988-US2969 19880826; NO 301770 B1 WO 1988-US2969 19880826, NO 1990-1229 19900316; NO 309001 B1 WO 1988-US2969 19880826, Div ex NO 1990-1229 19900316, NO 1994-2763 19940722

FDT FI 94357 B Previous Publ. FI 9001330; EP 397652 B1 Based on WO 8902445; DE 3855351 G Based on EP 397652, Based on WO 8902445; JP 2670996 B2 Previous Publ. JP 09183804; JP 2684208 B2 Previous Publ. JP 03502704, Based on WO 8902445; NO 301770 B1 Previous Publ. NO 9001229; NO 309001 B1 Previous Publ. NO 9402763

PRAI US 1987-100104 19870918

AB WO 8902445 A UPAB: 20010110

A method for making a water insoluble biocompatible gel comprises (a) activating **hyaluronic acid** (HA) with an activating agent and (b) reacting the activated HA with a nucleophile, under conditions producing the gel. The activating agent may be a carbodiimide e.g. 1-ethyl-3-(3-dimethylaminoropyl) carbodiimide (EDC) or 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide methiodide. The nucleophile may be an amino acid or salt, ester or amide, e.g. L-leucine methyl ester hydrochloride, L-phenylalanine hydrochloride or leucinamide hydrochloride or a monofunctional **amine**, e.g. aniline. Also claimed is a water insoluble compsn. comprising HA, the compsn. being free of **crosslinking**. Also claimed is a water insoluble compsn. comprising the reacting prod. of HA, an activating agent and a nucleophile. The compsns. may also contain a detectable marker e.g. Brilliant Blue R.

USE/ADVANTAGE - Because the gels and films made from the gels are biocompatible and water insoluble they are partic. useful as surgical aids where tissues are to be displaced or sepd. for an extended period of time such as e.g. a period of time sufficient to permit healing of a wound.

Dwg.0/0

| L Number | Hits | Search Text | DB | Time stamp |
|---|---|---|---|---|
| 1 | 0 | hyaluronic and (CH2n adj adj CH2n) | USPAT; US-PGPUB; EPO; JP ; DERWENT | 2002/09/30 15:47 |
| 2 | 181 | hyaluronic with (sulphated or sulfated) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 15:48 |
| 3 | 0 | (hyaluronic with (sulphated or sulfated)) and hemisuccinylated | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 15:49 |
| 4 | 0 | hyaluronic and hemisuccinylated | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 15:49 |
| 5 | 49 | hyaluronic with succinylated | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 15:56 |
| 6 | 0 | succinylated adj hyaluron$ | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 15:57 |
| 7 | 44 | (sulphated adj hyaluron$) or (sulfated adj hyaluron$) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 16:05 |
| 8 | 6 | ((sulphated adj hyaluron$) or (sulfated adj hyaluron$)) and diamine | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 16:05 |
| - | 16 | hyaluronic with (polyamine or diamine) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 15:46 |
| - | 3 | (hyaluronic with (polyamine or diamine)) and ((crosslinked adj hyaluronic) or (cross adj linked adj hyaluronic)) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 09:49 |
| - | 346 | hyaluronic and (crosslinked or (cross adj linked)) and (polyamine or diamine) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 10:26 |
| - | 7 | (hyaluronic and (crosslinked or (cross adj linked)) and (polyamine or diamine)) and hyaluronic.ti. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 11:12 |

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|---|---|---|---|---|
| - | 172 | (hyaluronic and (crosslinked or (cross adj linked)) and (p lyamine or diamine)) and (zinic or copper or iron) | USPAT; US-PGPUB; EP ; JP ; DERWENT | 2002/09/30 11:18 |
| - | 3 | ((hyaluronic and (crosslinked or (cross adj linked)) and (polyamine r diamine)) and hyaluronic.ti.) and (zinic or copper or iron) | USPAT; US-P PUB; EPO; JPO; DERWENT | 2002/09/30 13:01 |
| - | 2 | ("5616568").PN. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/30 13:01 |